

**“CYTOMORPHOLOGICAL EVALUATION OF NODULAR AND  
DIFFUSE THYROMEGALY WITH EMPHASIS ON BETHESDA  
SYSTEM OF REPORTING – A PROSPECTIVE STUDY”**

**DISSERTATION SUBMITTED TO  
THE TAMILNADU DR.M.G.R. MEDICAL UNIVERSITY  
CHENNAI**

*in partial fulfilment of  
the requirements for the degree of*

**M.D. (PATHOLOGY)**

**BRANCH - III**



**TIRUNELVELI MEDICAL COLLEGE HOSPITAL**

**TIRUNELVELI**

**APRIL-2015**

## **CERTIFICATE**

This is to certify that this Dissertation entitled **“CYTOMORPHOLOGICAL EVALUATION OF NODULAR AND DIFFUSE THYROMEGALY WITH EMPHASIS ON BETHESDA SYSTEM OF REPORTING – A PROSPECTIVE STUDY”** is the bonafide original work of **Dr.M.UMA DEVI**, during the period of her Post graduate study from 2012 – 2015, under my guidance and supervision, in the Department of Pathology Tirunelveli Medical College & Hospital, Tirunelveli, in partial fulfillment of the requirement for M.D., (Branch III) in Pathology examination of the Tamilnadu Dr.M.G.R Medical University will be held in April 2015.

**The DEAN**

**Tirunelveli Medical College,  
Tirunelveli - 627011.**



## **CERTIFICATE**

I hereby certify that this dissertation entitled **“CYTOMORPHOLOGICAL EVALUATION OF NODULAR AND DIFFUSE THYROMEGALY WITH EMPHASIS ON BETHESDA SYSTEM OF REPORTING – A PROSPECTIVE STUDY ”** is a record of work done by **Dr. M.UMA DEVI**, in the Department of Pathology, Tirunelveli Medical College, Tirunelveli, during her postgraduate degree course period from 2012- 2015. This work has not formed the basis for previous award of any degree.

**Dr.K.Swaminathan, M.D**

Professor of Pathology,  
Department of Pathology,  
Tirunelveli Medical College,  
Tirunelveli -11

**Dr.K.Shantaraman, M.D**

Professor and HOD of Pathology,  
Department of Pathology,  
Tirunelveli Medical College,  
Tirunelveli -11



**TIRUNELVELI MEDICAL COLLEGE**

**TIRUNELVELI,**

**STATE OF TAMILNADU, INDIA**

**PIN CODE: 627011**

**Tel: 91-462-2572733, 2572734 Fax: 91-462-2572944**

**Estd: 1965**

**Under the Directorate of Medical Education, Government of Tamilnadu.**



## **Institutional Ethical Committee**

### **Certificate of Approval**

This is to certify that the Institutional Ethical Committee of this College unanimously approves the Thesis /Dissertation/ Research Proposal submitted before this committee by Dr.M.Uma Devi, Post Graduate in Pathology, Department of Pathology, Tirunelveli Medical College /Hospital, Tirunelveli titled **"CYTOMORPHOLOGICAL EVALUATION OF NODULAR AND DIFFUSE THYROMEGALY WITH EMPHASIS ON BETHESDA SYSTEM OF REPORTING - A PROSPECTIVE STUDY"** registered by the IEC as 298/PATHO/IEC/2012 dated 14.12.2012. The Investigator is hereby advised to adhere to all the stipulated norms and conditions of this ethical committee.

Issued on this Date

**14.12.2012**

Under Seal



*[Signature]*  
Secretary,  
Ethical Committee,  
Tirunelveli Medical College,  
Tirunelveli-11.

1

**"CYTOMORPHOLOGICAL EVALUATION OF NODULAR AND  
DIFFUSE THYROMEGALY WITH EMPHASIS ON BETHESDA  
SYSTEM OF REPORTING - A PROSPECTIVE STUDY"**

**DISSERTATION SUBMITTED TO**

**THE TAMILNADU DR. MGR. MEDICAL UNIVERSITY**

**CHENNAI**

**in partial fulfillment of**

**the requirements for the degree of**

**M.D. (PATHOLOGY)**

**BRANCH - III**



Match Overview

1	Lesley J. Lloyd Submitted	1%
2	Lesley J. Lloyd Submitted	1%
3	Wang, Fain Submitted	1%
4	Lesley J. Lloyd Submitted	1%
5	Lesley J. Lloyd Submitted	<1%
6	Lesley J. Lloyd Submitted	<1%
7	Lesley J. Lloyd Submitted	<1%
8	Submitted to Higher Ed Submitted	<1%

## **DECLARATION**

I solemnly declare that this dissertation titled **“CYTOMORPHOLOGICAL EVALUATION OF NODULAR AND DIFFUSE THYROMEGALY WITH EMPHASIS ON BETHESDA SYSTEM OF REPORTING – A PROSPECTIVE STUDY ”** submitted by me for the degree of M.D, is the record work carried out by me during the period of 2012-2015 under the guidance of **Prof. Dr.K.SWAMINATHAN**, Professor of Pathology, Department of Pathology, Tirunelveli Medical College, Tirunelveli. The dissertation is submitted to The Tamilnadu Dr. M.G.R. Medical University, Chennai, towards the partial fulfilment of requirements for the award of M.D. Degree (Branch III) Pathology examination to be held in April 2015.

Place: Tirunelveli

Date:

**DR.M.UMA DEVI,**

Department of Pathology,  
Tirunelveli Medical College,  
Tirunelveli-11.

## ACKNOWLEDGEMENT

I take immense pleasure at this opportunity to acknowledge all those who have helped me to make this dissertation possible.

I express my heartfelt thanks to the **Dean, Tirunelveli Medical College**, for permitting me to undertake this study. I express my profound sense of gratitude to **Dr.K.Shantaraman ,MD.**, my respected Professor and Head of Department of Pathology, Tirunelveli Medical College, Tirunelveli, for his valuable advice, constant guidance and motivation in the preparation of this work.

I consider it my privilege and honour to have worked under the unstinted guidance, encouragement, and supervision of my respected guide **Dr.K.Swaminathan ,MD.**, Professor of Pathology.

I thank **Dr.S.Vallimanalan MD, Dr.J.Suresh Durai, MD., Dr.Arasi Rajesh, MD.**, Professors of Pathology, for their constant support and inspiration. I also thank the Assistant Professors, for their encouragement and support. I sincerely thank the Professors and faculties of the Department of General Surgery for providing me the patients for my study. I take this opportunity to thank all my postgraduate colleagues for their valuable support.

My thanks to all the technicians and other members of the Department of Pathology for their kind help at different stages of this study.

**Dr.M.Uma Devi**

## **LISTS OF ABBREVIATIONS USED**

FNAC	-	Fine needle aspiration cytology
TBSRTC	-	The Bethesda system of reporting thyroid cytopathology
ND /UNS	-	Non- diagnostic/Unsatisfactory
AUS/FLUS	-	Atypia of undetermined significance/ Follicular lesion of undetermined significance
FN/SFN	-	Follicular neoplasm/ Suspicious for follicular Neoplasm
SFM	-	Suspicious for malignancy
CAT –I	-	Category I
BFN	-	Benign follicular nodule
FNHCT	-	Follicular neoplasm of Hurthle cell type
SFNHCT	-	Suspicious for Follicular neoplasm of Hurthle cell type
HCN	-	Hurthle cell nodule
MEN	-	Multiple endocrine neoplasia
FMTc	-	Familial medullary thyroid carcinoma
MTC	-	Medullary thyroid carcinoma
CEA	-	Carcino embryonic antigen
HMB-45	-	Human melanoma black -45
TTF-1	-	Thyroid transcription factor -1

## **TABLE OF CONTENTS**

<b>S.NO</b>	<b>TITLES</b>	<b>PAGE NO</b>
<b>1</b>	<b>INTRODUCTION</b>	<b>1</b>
<b>2</b>	<b>AIMS AND OBJECTIVES</b>	<b>3</b>
<b>3</b>	<b>REVIEW OF LITERATURE</b>	<b>4</b>
<b>4</b>	<b>MATERIALS AND METHODS</b>	<b>47</b>
<b>5</b>	<b>OBSERVATION AND RESULTS</b>	<b>49</b>
<b>6</b>	<b>DISCUSSION</b>	<b>87</b>
<b>7</b>	<b>SUMMARY</b>	<b>106</b>
<b>8</b>	<b>CONCLUSION</b>	<b>108</b>

**BIBLIOGRAPHY**

**APPENDIX**

**MASTER CHART**

## ABSTRACT

Swelling in thyroid are frequently encountered . Clinical evaluation helps in diagnosis but is difficult to distinguish the early malignant lesions from the more prevalent benign goiters. FNAC is a simple and safe procedure , carried out in OPD with minimum equipment and has good patient compliance . As FNAC is the primary investigation for the management of thyroid lesions , its interpretation is very crucial . This study aims at classifying the cytomorphological profile of nodular and diffuse thyromegaly cases with emphasis on Bethesda system of reporting. The Bethesda System for Reporting Thyroid Cytopathology ( TBSRTC) is used for clarity of communication and recommends that each case should be reported in 1 of 6 diagnostic categories which include Category I –Non –diagnostic , Category II- Benign, Category III- Atypia of undetermined significance/ Follicular lesion of undetermined significance (AUS/FLUS) ,Category IV- Follicular neoplasm / Suspicious for follicular neoplasm (FN/SFN), Category V- Suspicious for malignancy (SFM), Category VI – Malignant, thus facilitating a uniform communication among the managing team of doctors and leaves no confusion regarding the management of thyroid lesions.

A total of 300 cases with thyroid swellings were studied during the period of January 2013 to June 2014 . FNAC of thyroid was done in all cases and the cytomorphology of the individual thyroid lesions were evaluated



and all cases were reported using TBSRTC. Of the total 300 cases , 3 cases(1%) were reported in category I , 274 cases (91.3%) were reported in category II , 1 case(0.3%) in category III , 12 case ( 4%) in category IV , 2 cases (0.7%) in category V, 8 cases (2.7%) in category VI. Major bulk of cases were seen in category II.

Thus the application of TBSRTC bridges the gap in communication between the clinicians and helps in the proper patient management .

**Keywords :** FNAC, thyroid lesions , Bethesda

## INTRODUCTION

Thyroid lesions are one of the common clinical conditions being encountered in clinical practice and are different from other diseases in terms of their ease of diagnosis, accessibility of medical treatment, and the relative visibility of the swelling that even a small swelling of the thyroid offers to the treating physician. Early diagnosis and treatment remains the cornerstone of management.

The annual incidence of thyroid malignancy ranges from 0.5 to 10 cases per 1,00,000 population.<sup>[1]</sup> With a wide spectrum of disorders and a considerable degree of variation in its presentation, it is often difficult to arrive at a correct diagnosis by clinical evaluation alone. So it is essential to have a battery of test done which include: thyroid hormonal profile, ultrasound imaging studies and Fine Needle Aspiration Cytology.

Fine Needle Aspiration Cytology is an outpatient procedure which is used as a primary investigation in the diagnosis of thyroid swellings. It is a simple, speedy, safe, cost effective and accurate technique being used worldwide for evaluation of thyroid swellings. The clinical value of thyroid FNAC is useful in the diagnosis of inflammatory, infectious and neoplastic conditions.<sup>[2]</sup>

As FNAC defines the difference between the benign and cancerous lesions very accurately therefore it is used as a best screening tool in the preoperative diagnosis through the world.

The thyroid nodules have a reported prevalence of 4 to 7% in the general population.<sup>[3-6]</sup> Thyroid cancer is the most common type of endocrine malignancy. It constitutes 1.7% of all newly diagnosed cancer cases worldwide. The incidence of thyroid cancer is about three times higher among females than males.<sup>[7]</sup>

The incidence of thyroid cancer is rare in children, but its incidence begins to rise sharply in the second decade of life and peaks during the fifth and sixth decades of life. Papillary carcinoma of thyroid constitutes ~ 80% of all thyroid cancer cases, follicular carcinoma (15%), and medullary carcinoma (3%). Anaplastic carcinoma which accounts for < 2% of thyroid tumors, typically occurs in the older age group and its incidence continues to rise with age.<sup>[7]</sup>

This study aims at classifying the cytomorphological profile of nodular and diffuse lesions of thyroid under the standardized Bethesda system of reporting thereby establishing its role in proper diagnosis and maintaining a uniform communication among different clinicians to avoid confusion and thus helps in proper patient management.

## **AIMS AND OBJECTIVES**

A prospective study is carried out on fine needle aspiration cytology of thyroid lesions with the following objectives.

1. To study the cytomorphological features of aspirated material from various thyroid lesions like nodular and diffuse thyromegaly.
2. To correlate the cytomorphological features and classify the thyroid lesions with emphasis on Bethesda system of reporting.
3. To study the utility of the Bethesda system of reporting

## **REVIEW OF LITERATURE**

### **EMBRYOLOGY**

The thyroid gland develops as an outpouching of the primitive foregut in early weeks of gestation at the site of foramen caecum in the base of the tongue. The endoderm cells which are seen lining the floor of pharyngeal anlage thicken and form the median thyroid anlage. The thyroid gland descends in the midline as a component of the thyroglossal duct to reach its final position in the mid neck. The second branchial arch forms the hyoid bone. The thyroglossal duct is situated anterior to the hyoid bone and is divided by the hyoid bone into a suprahyoid and an infrahyoid portion. In due course the thyroglossal duct is obliterated and leaves a vestige of pyramidal lobe in 40% of individuals. The paired lateral anlagen originate from fourth branchial pouch and fuse with median anlage at fifth week of gestation.<sup>[8]</sup>

The lateral anlagen are neuroectodermal in origin (ultimobranchial bodies) and contain the parafollicular or C cells which produce calcitonin<sup>[9]</sup> The cords and plates of thyroid follicular cells are formed by the end of the 9<sup>th</sup> week, the small follicular lumen is formed by 10<sup>th</sup> week, the colloid secretion occurs by 12<sup>th</sup> week and thyroglobulin positive colloid in lumen by 14<sup>th</sup> week.<sup>[10]</sup>

The development of the thyroid gland is controlled by specific transcription factors such as TTF-1, TTF-2, PAX8, HHEX and their altered expression plays a role in thyroid dysgenesis.<sup>[11]</sup>

## **ANATOMY**

Thyroid gland is placed in front of the neck, anterior to the trachea and composed of two lobes which are connected by isthmus. The two lobes of the thyroid are divided by fibrous septa into lobules, and each lobule contains about 30 to 40 follicles. The whole thyroid gland is enclosed in a true capsule. Mature thyroid gland measures about 6×3×2 cms approximately and weighs about 25-30 gms. Thyroid gland is a highly vascular structure and it is supplied by subclavian artery and carotid artery. There are four pea sized parathyroid glands embedded posteriorly in superior and inferior pole of thyroid gland.<sup>[8]</sup>

## **HISTOLOGY**

The follicles in thyroid gland are round to oval with an average diameter of 200 µm lined by thyroid follicular cells. The follicles in thyroid are often filled with colloid which is described as a homogenous eosinophilic material. There are variations in the density and in the staining properties of the colloid according to the different clinical conditions. The presence of thin eosinophilic colloid indicates that the gland is functionally active and the presence of thick eosinophilic colloid appears to be associated with inactive follicles and is also seen in some malignant conditions of thyroid. The appearance of follicular cells depends on the functional activity of the thyroid gland.<sup>[8]</sup>

## **PHYSIOLOGY**

The main function of thyroid gland is secretion of thyroid hormones and calcitonin. Regulation of thyroid function is by the hormone TSH which is secreted from the anterior pituitary. The lesions in thyroid are largely divided into two major types: the lesions that show a diffuse pattern and the lesions that are associated with nodular pattern. The nodules in turn can be divided into solitary or multiple.

## **CLASSIFICATION OF THYROID SWELLING <sup>[12]</sup>**

### **1. SIMPLE GOITRE(EUTHYROID)**

Diffuse hyperplastic - (Physiological, Pubertal, Pregnancy)

Multinodular goitre

### **2. TOXIC**

Diffuse (Grave's disease)

Multinodular (Toxic adenoma)

### **3. INFLAMMATORY**

Autoimmune - Hashimoto's thyroiditis

- Classic lymphocytic thyroiditis

Granulomatous - De Quervain's thyroiditis

Fibrosing - Riedel's thyroiditis

Infective - Acute (bacterial thyroiditis, viral thyroiditis,)

- Chronic (tuberculosis, syphilis)

### **4. NEOPLASTIC**

## **NON –NEOPLASTIC LESIONS OF THYROID**

### **DIFFUSE NON TOXIC (SIMPLE) GOITER OR COLLOID GOITER**

The other names of this goitre include adenomatous goiter, diffuse or nodular goiter, endemic goiter, multinodular goitre. This type of goitre is usually caused by hyperplasia of the thyroid gland which is induced by iodine deficiency. In the early stages of this lesion there is a diffuse enlargement of the gland, which is made up of small follicles. In later stages, some of the follicles may become distended and may coalesce to form nodules ranging in various sizes. The degenerative changes, usually occur in the nodules such as haemorrhage, necrosis, cyst and scar formation. The colloid goitre is the most common lesion which is often referred for aspiration. The colloid appears as pink homogeneous material in microscopy and is usually surrounded by a few follicular cells.

### **GRAVE'S DISEASE <sup>[16]</sup>**

It is a form of primary thyroid hyperplasia. The aspirates in this disease presents with moderate to high cellularity and a colloid-free bloody background. The follicular cells are arranged in monolayered sheets or can be arranged in follicles. The cytoplasm is moderate in amount and is pale in color and vacuolated.



## **INFLAMMATORY LESIONS**

### **ACUTE THYROIDITIS**

It can be suppurative or nonsuppurative. The etiology can be bacterial, fungal or it may be associated with radiation and is usually of infectious nature.<sup>[13]</sup>

### **HASHIMOTO'S THYROIDITIS**

It is the most common cause of autoimmune thyroiditis reported by Hakaru Hashimoto in 1912. The other name of this thyroiditis is “ Struma lymphomatosa”. The etiology is mostly due to effect of autoantibodies that alter the thyroid function. The immune-mediated injury of the thyroid gland leads to diffuse or nodular enlargement of the gland and then leading to exhaustion atrophy which is then manifested by diffuse oxyphilia of the follicular epithelium. The etiological factors leading to autoimmune thyroiditis are of both humoral and cellular nature. There are circulating autoantibodies which are present against thyroglobulin and other follicular cell antigens, and other thyroid follicle receptors like thyrotropin (TSH) receptors. The main etiology of this type of thyroiditis is due to organ-specific defect in suppressor T lymphocytes. Therefore it is concluded that the etiology of autoimmune thyroiditis is multifactorial and is therefore of variable penetrance.<sup>[14]</sup>

The smears in this type of thyroiditis composed of mixture of lymphocytes and oncocytes or Hürthle cells. The smear in Hashimoto's

thyroiditis may resemble an aspirate of a hyperplastic lymph node. There is striking, abundant, eosinophilic and granular cytoplasm and there is variability in nuclear sizes. The nuclei contains large nucleoli and contain large intranuclear cytoplasmic inclusions. Sometimes the follicular cells in clusters may mimic a papillary carcinoma.

The 'lymphocytic' type of HT is mostly seen in children and young adults. The smears show characteristic reactive lymphoid proliferation. The histiocytes have abundant amount of pale cytoplasm with granular chromatin. The florid type of HT occurs in older individuals who are hypothyroid.

The aspirate smear shows lymphocytes admixed with variable number of plasma cells. There is prominent oxyphilic change.

### **SUBACUTE GRANULOMATOUS THYROIDITIS (De QUERVAIN'S)**

This type of thyroiditis is probably of viral etiology and is of self limiting in nature. It occurs predominantly in females usually in the second to third decade of life after a respiratory infection and presents with clinical symptoms like sore throat, painful deglutition, and marked tenderness on palpation in the thyroid region, and often associated with fever and malaise. Histologic examination shows areas of marked inflammation and granulomas containing foreign body type of giant cells. The Smears in Granulomatous thyroiditis shows large multinucleate giant cells having numerous nuclei and granulomatous aggregates of epithelioid cells, and

degenerating follicular cells, neutrophils, macrophages and lymphocytes in a dirty smear background that shows debris.

## **REIDEL'S THYROIDITIS**

This type of thyroiditis presents with an extensive sclerosis of the thyroid gland. The sclerosis is sometimes also associated with a similar tissue reaction in the mediastinum, retroperitoneum, and orbit. The consistency of thyroid gland is rubbery or firm and the aspirations are very minimal due to extensive desmoplastic reaction in the thyroid stroma. Due to its firm nature this type of thyroiditis must be differentiated from infiltrating carcinoma. <sup>[2] [15]</sup>

## **TUMORS OF FOLLICULAR OR METAPLASTIC EPITHELIUM**

### **FOLLICULAR ADENOMA**

Follicular adenoma is the most common type of thyroid neoplasm and lacks evidence of capsular or vascular invasion. <sup>[10]</sup> The aspirates are cellular with little colloid. The smears contain large clusters of follicular cells arranged in flat follicular or papillary structures or aggregates. The tumor cells may also form small rosette-like acinar clusters containing inspissated colloid. Single follicular cells and nuclei stripped of cytoplasm ("naked nuclei") are seen scattered throughout the smear. The anisonucleosis may be present.

## **PAPILLARY CARCINOMA**

They are the most common malignant tumors of the thyroid and usually presents as a palpable thyroid nodule. These malignancies are predominantly seen in females but sometimes may be seen in males and few cases also present in children. The smears are very cellular and the pattern of arrangement is predominantly in anastomosing papillary fragments but can be arranged as follicular structures, or in monolayered sheets generally free of colloid. The papillary pattern of arrangement is diagnostic of this tumor. It is common to find psammoma bodies in this cancer. The individual tumor cells, are usually larger. The cytoplasm is basophilic with sometimes discrete vacuoles can be seen. The nuclear features are very characteristics for this malignancy. The common nuclear features is the prescence of “ground-glass” nuclei and small central nucleoli. There is prescence of intranuclear cytoplasmic inclusions. Another characteristic nuclear feature is the prescence of nuclear grooves. The most important diagnostic feature is prescence of intracytoplasmic nuclear inclusions. The variants of papillary carcinoma include :

1. Cystic papillary carcinoma.
2. Follicular variant of papillary carcinoma.
3. Tall-cell variant of papillary carcinoma.
4. Warthin's-like variant of papillary carcinoma.
5. Diffuse sclerosing variant of papillary carcinoma in childhood.

## **FOLLICULAR CARCINOMA**

It is a rare neoplasm of thyroid showing invasion of capsule, blood vessels, or adjacent thyroid parenchyma. It also has predilection for women. The smears are cellular. Its microscopic appearance ranges from well formed follicles to solid growth pattern.<sup>[10]</sup> Thus, they may closely resemble the cytologic feature of follicular adenoma. In the well-differentiated form of follicular carcinoma, cellular atypia is minimal, and the smear may suggest a benign lesion. In such cases, the cytologic diagnosis should be “follicular neoplasm or tumor,” clearly indicating that surgical excision and histologic examination is mandatory for a confirmed diagnosis.

## **HURTHLE CELL (ONCOCYTIC) TUMORS**

Tumors in this category are composed of > 75% of follicular cells exhibiting oncocytic features. Most patients are adults, with a predominance in females.<sup>[10]</sup> The majority are benign and are designated as Hurthle cell adenoma. In aspirations the cells are of uniform size and shape and they form tight clusters. The nuclei are large, vary in size, and may contain visible nucleoli. The most important differential diagnosis of Hürthle cell tumor is Hashimoto's thyroiditis with little or no lymphocytic component. Tumors with clear capsular or vascular invasion are called as Hurthle cell carcinoma.<sup>[2]</sup>

## **POORLY DIFFERENTIATED (INSULAR ) CARCINOMA**

This tumor occurs in older age but can occur in adolescents also. This tumor shows a characteristic nesting (insular) pattern, small uniform tumor cells, variable mitotic activity, tumor necrosis resulting in a peritheliomatous pattern.<sup>[10]</sup>

## **UNDIFFERENTIATED CARCINOMA**

This tumor most commonly presents in older individuals. Extrathyroidal extension is present in most cases. There are two forms of anaplastic carcinoma: a giant cell carcinoma and a small-cell-type carcinoma.<sup>[2]</sup> Smears of aspirates from the anaplastic giant cell carcinoma contain usually necrotic matter, cellular debris, inflammatory cells, mainly granulocytes, and large polymorphous, often multinucleated cells with large bizarre nuclei and very prominent nucleoli and in the small-cell variant of anaplastic carcinoma, the aspirate contains malignant cells with round or oval nuclei and scanty cytoplasm.<sup>[2] [10]</sup>

## **MEDULLARY CARCINOMA**

It is a distinctive type of thyroid tumour composed of C(parafollicular) cells. The various morphological presentation of cell include plasmacytoid, small cell, spindle cell. Moderate anisonucleosis may be present and contains scattered large nuclei, which can be binucleate and multinucleate forms, there is 'neuroendocrine' type of uniform, stippled nuclear chromatin. The stroma is often vascular and contains hyalinised collagen and amyloid<sup>[2] [10]</sup>

## **LYMPHOMA**

The primary lymphomas of thyroid, are of B-cell derivation, and is seen in patients with Hashimoto's thyroiditis. The smear contains lymphoma cells admixed with epithelial components. The majority of lymphomas arise primarily in the gland itself but may later involve lymph nodes and other organs.

## **METASTATIC TUMORS IN THYROID**

The clinical presentation under this category can present as nodular or diffuse pattern. In nodular presentation the nodules can present as single or multiple or the metastasis can involve the whole gland and present in a diffuse pattern involving the entire gland. The metastases may sometimes mimic primary tumors of the thyroid. The distinction between a metastasis and primary thyroid tumor may sometimes be difficult. For example, in metastatic renal cell carcinoma cells may be elongated, or spindle in shape which mimics the cells seen in medullary carcinoma.

If the malignant cells in the aspirate demonstrates cytologic features like keratinization, the presence of mucin, the presence of melanin, or cells with abundant clear cytoplasm, which are usually not seen in primary tumors of thyroid a diagnosis of metastasis may be suggested.

**[TABLE 1]: Approximate percentage of various thyroid malignancies<sup>[1]</sup>**

TYPE OF MALIGNANCY	PERCENTAGE
Papillary carcinoma	70-80 %
Follicular carcinoma	10-20%
Medullary carcinoma	5-10%
Anaplastic carcinoma	2-10%
Poorly differentiated carcinoma	0.4-10%
Lymphoma	4-5 %

Expressed as the proportions of all thyroid malignancies

The above table shows the distribution of percentage of various thyroid malignancies encountered.

### **FINE NEEDLE ASPIRATION CYTOLOGY**

It is one of the primary investigation used for the management of thyroid lesions, and its interpretation is very crucial for diagnosis<sup>[18]</sup>.

### **HISTORICAL HIGHLIGHTS**

FNA has been shown to be the safest and most accurate of diagnostic tools in thyroid lesions.<sup>[19]</sup> The fine needle aspiration method for studying thyroid was first done in Sweden in 1950s and its utility as a diagnostic protocol was established.<sup>[20]</sup> Imprints during frozen section are very useful in identification of follicular variant of papillary carcinoma (FV-PC) as the characteristic nuclear morphology is better seen by this procedure.<sup>[21]</sup> The US-guided FNA of thyroid is especially useful in cystic and multinodular



lesions harboring malignancy.<sup>[22]</sup> Various modifications have been introduced to the Fine needle aspiration cytology technique. Santos JEC and Leiman G in 1988 pioneered a technique, non aspiration of fine needle cytology to study nodular lesions. This technique eliminates the active aspiration which is replaced by the principle of capillary suction of fluid or semisolid material into thin channel of the needle.<sup>[23]</sup> Another development is the ultrasound guided FNAC which has proved to be beneficial in non - palpable nodules. Liquid based preparation is advocated as an adjunct to conventional smears. Its main advantages are reduction in number of slides to be screened, ability to perform immunocytochemical and other special stains and enhancement of nuclear details and irregularities of papillary carcinoma.

Orell has defined the main indications for thyroid FNAC, they are <sup>[24]</sup>

1. Diagnosis of diffuse non – toxic goitre.
2. Diagnosis of solitary thyroid nodule.
3. Confirmation of a malignancy.
4. To obtain material for defining prognostic parameters.

#### **ADVANTAGES OF FNAC**

1. The technique is simple, safe, cost effective and can be done as an out patient procedure.
2. Time required is very less and it's interpretation is rapid.

3. Representative sample is drawn, while maintaining steady suction in various areas of the nodule.
4. Cysts can be aspirated completely and thus it acts as a therapeutic procedure for the patient.
5. Its main purpose is to provide a rational approach to management.

### **DISADVANTAGES OF FNAC**

Minimal material available for examination. Architecture, cell relationship are absent.<sup>[25]</sup>

1. The needle may miss important areas of the nodule despite a good attempt for a representative smear by aspiration from different areas.
2. Distinction between a follicular adenoma and follicular carcinoma is difficult.<sup>[26]</sup>

### **COMPLICATIONS**

FNAC is considered simple and safe procedure. It is rarely associated with complications as described below.<sup>[27]</sup>

1. Local discomfort.
2. Minor hematoma.
3. Puncturing carotid artery, internal jugular vein, which is very rare.
4. Seeding of tumour along the needle track, though theoretically possible, the reported cases in world literature are anecdotal.<sup>[28, 29]</sup>
5. Transient nerve palsy.<sup>[30]</sup>

## **PITFALLS OF FNAC**

1. Inadequate sampling : The aspirate may be cell poor as in Reidel's thyroiditis and a second attempt becomes mandatory.
2. Geographical misses: In such cases prior ultrasound may delineate the area of interest.

The lack of a standardized reporting format has caused confusion and ambiguity in interpreting FNAC results. To address this need, the 2007 National Cancer Institute State of the Science Conference proposed a uniform classification scheme named Bethesda with 6 distinct diagnostic categories for classifying the various thyroid disorders.

## **THE BETHESDA SYSTEM OF THYROID CYTOPATHOLOGY**

### **[TABLE-2]**

The National cancer institute (NCI) hosted the State Of Science Conference on thyroid fine needle aspiration. The meeting took place on October 22 and 23, 2007, in Bethesda. The result of the meeting proposed a uniform classification system for identifying the thyroid lesions and named the classification as Bethesda system for reporting thyroid cytology which had six diagnostic categories as mentioned in [TABLE-2].<sup>[32]</sup>

The Bethesda system recommends that each thyroid FNA should be reported under this classification to avoid confusion in management and to have a uniform communication between different clinicians as each category has its own implied cancer risk and each category is managed separately.[TABLE -2]

***[TABLE -2 ] : The Bethesda system of classification***

<b>CATEGORY I</b>	<b>Non -diagnostic/ Unsatisfactory</b>	<b>Cyst fluid only</b>
		<b>Virtually Acellular smear</b>
		<b>Others (Obscuring blood/Drying artefact)</b>
<b>CATEGORY II</b>	<b>Benign</b>	<b>Consistent with benign follicular nodule (Adenomatoid nodule, colloid nodule etc)</b>
		<b>Consistent with lymphocytic (Hashimoto) thyroiditis in proper clinical context</b>
		<b>Consistent with granulomatous (subacute ) thyroiditis</b>
		<b>Other</b>
<b>CATEGORY III</b>	<b>Atypia of undetermined significance or follicular lesion of undetermined significance</b>	
<b>CATEGORY IV</b>	<b>Follicular neoplasm/ suspicious of follicular neoplasm</b>	
<b>CATEGORY V</b>	<b>Suspicious for malignancy</b>	<b>Suspicious for papillary carcinoma</b>
		<b>Suspicious for medullary carcinoma</b>
		<b>Suspicious for metastatic carcinoma</b>
		<b>Suspicious for lymphoma</b>
		<b>Other</b>
<b>CATEGORY VI</b>	<b>Malignant</b>	<b>Papillary thyroid carcinoma</b>
		<b>Poorly differentiated carcinoma</b>
		<b>Medullary thyroid carcinoma</b>
		<b>Undifferentiated (anaplastic carcinoma)</b>
		<b>Squamous cell carcinoma</b>
		<b>Carcinoma with mixed features</b>
		<b>Metastatic carcinoma</b>
		<b>Non – Hodgkin lymphoma</b>

## **CRITERIA FOR ADEQUACY**

A thyroid FNA sample is considered adequate for evaluation if it contains a minimum of six clusters of well visualized thyroid follicular cells, and there should be atleast ten cells per cluster.

## **NON DIAGNOSTIC- UNSATISFACTORY FOR EVALUATION**

A specimen is considered Non – diagnostic <sup>[31]</sup> if it does not contain the adequate clusters recommended for a definite diagnosis. An adequate FNA smear contains a minimum of six clusters of well visualized thyroid follicular cells, with atleast ten cells per cluster, a smear is considered non-diagnostic when it fails to meet the adequacy criteria. Few cystic lesions are also considered non-diagnostic when it shows only cyst macrophages and very fewer benign thyroid follicular cells.

## **BENIGN FOLLICULAR NODULE [BFN]**

This smear contains predominantly of colloid and benign-appearing thyroid follicular cells. The other terms like colloid nodule, nodular goiter adenomatoid nodule, Graves' disease are used depending upon the clinical presentation and features of thyroid follicular cells. The sample is moderately cellular, and when colloid is present it can be thick or thin and has a viscous or shiny appearance, or sometimes have brown color in nature. The prescence of colloid gives a definite background to the smear, thin colloid gives a crazy pavement like background and thick colloid gives a cracking artefact like appearance to the smear.<sup>[32]</sup>

The arrangement of thyroid follicular cells is predominantly in monolayered sheets sometimes the follicular cells may be seen arranged in clusters also. The individual follicular cells have moderate amounts of cytoplasm with dark, round to oval nuclei and a granular chromatin. Anisonucleosis if present is very mild. The abundance of colloid with honeycomb-like arrangement of follicular cells and occasionally admixed with few Hurthle cells if any is the hallmark of BFN.

Sometimes the smear in BFN contains thyroid follicular cells which have nuclear features suggestive of a papillary thyroid carcinoma. Such smears are better interpreted as “Suspicious for malignancy” or “Atypia of Undetermined Significance (AUS)”, depending on the extent of atypia.<sup>[33,34,35]</sup>

## **GRAVE’S DISEASE**

It is a diffuse hyperplastic thyroid disorder which is mostly autoimmune, mainly seen in middle-aged females and presents with features of hyperthyroidism. The smears are cellular admixed with lymphocytes, oxyphilic cells. The pattern of arrangement of follicular cells is seen in flat sheets and loose groups, the individual thyroid follicular cells have abundant cytoplasm and there is often enlarged nuclei sometimes it can be vesicular with prominent nucleoli.<sup>[36]</sup>

## **LYMPHOCYTIC (HASHIMOTO'S ) THYROIDITIS**

This thyroiditis is mostly seen in middle-aged females. The clinical presentation is mostly diffuse enlargement of thyroid, but sometimes can present as nodular swelling which then warrants a FNAC to be done.

### **DEFINITION**

The term “Consistent with lymphocytic (Hashimoto’s) thyroiditis” refers to a smear which is exclusively composed of many lymphocytes admixed with few Hurthle cells along with the thyroid follicular cells.<sup>[37]</sup>

### **CRITERIA**

The smears are hypercellular. In this diagnostic category a minimum number of follicular/Hürthle cells is not needed for adequacy to interpret.<sup>[38]</sup> There is polymorphic lymphoid population admixed with occasional plasma cells and germinal center like lymphoid follicles may be seen sometimes in the background smear. The oxyphilic cells if they are present, they are usually arranged in sheets or seen as isolated cells. The oncocytes have abundant granular cytoplasm, large nuclei, and prominent nucleoli sometimes mild anisonucleosis is seen.

## **GRANULOMATOUS (SUBACUTE/De QUERVAIN’S THYROIDITIS)**

This is a inflammatory condition of thyroid which is usually self – limited and diagnosed on clinical routine. There is usually a diffuse presentation but when nodularity is present an FNA is generally performed in the patient. However the cytologic findings are nonspecific if there is

absence of granulomas. Due to inflammatory condition the biopsy procedure may be quite painful for the patient and thus leading to inadequate sampling.

## **CRITERIA**

There is variable cellularity and the cellularity depends on the stage of disease. There is presence of clusters of epithelioid histiocytes.<sup>[39]</sup> Different stages of presentation depends on different features in smears. In early stage of this type of thyroiditis there is lot of neutrophils seen in the smear and it resembles as that of acute thyroiditis and in the later stages the samples are hypocellular and they show giant cells surrounding the colloid and sometimes seen engulfing it , epithelioid cells, lymphocytes, macrophages, and scant degenerated follicular cells are also seen.<sup>[39]</sup> In the involutional stage of this disease the giant cells and inflammatory cells are absent in the smear.

## **ACUTE THYROIDITIS**

This type of thyroiditis is most commonly seen in immunocompromised individuals and is considered as a infectious condition of thyroid and with very rare presentation.

## **CRITERIA**

The smears are dominated by the presence of numerous neutrophils which are seen admixed with necrosis, fibrin, macrophages in a haemorrhagic background in the background of few scant reactive follicular cells.



## **RIEDEL'S THYROIDITIS**

This type of thyroiditis is very rare in presentation and there is extensive fibrosis of the thyroid and also involving the adjoining area in the neck thus leading to a consistency which is firm to stony hard.

### **CRITERIA**

Due to the fibrosis involving the gland the cellularity is very scant and almost acellular in many. The smear shows few spindle cells admixed with collagen. Sometimes rare inflammatory cells may be seen in the smear. The thyroid follicular cells are almost absent in the smear. Colloid is also not discernible in the smear.

## **ATYPIA OF UNDETERMINED SIGNIFICANCE / FOLLICULAR LESION OF UNDETERMINED SIGNIFICANCE**

### **DEFINITION**

This term is used when the thyroid follicular cells show nuclear atypia and arranged in its own architectural pattern so that it becomes difficult to classify the lesions in any definite category like follicular neoplasm, suspicious for follicular neoplasm, suspicious for malignancy and malignant category. The patients diagnosed under this category are followed up periodically and a repeat aspiration/ biopsy is recommended after a specific period of time.<sup>[40]</sup>

## CRITERIA

An AUS interpretation is appropriate in the cytological conditions which are mentioned below:

1. When the smear shows a predominant clusters of microfollicles but the cellularity is very little so that it does not fulfill the criteria for “Follicular Neoplasm/Suspicious for Follicular neoplasm, or when the sample is markedly cellular but the proportion of microfollicles is not adequate to classify the lesion under the category of “Follicular Neoplasm/Suspicious for Follicular Neoplasm.”<sup>[41]</sup>
2. The aspirate is very sparse and contains scant colloid admixed with a predominant population of Hürthle cells.
3. Prescence of artefact interfering with follicular cell atypia like the air-drying artefact which causes a slight nuclear and cytoplasmic enlargement and the clotting artifact associated with cellular crowding.
4. When there is predominant population of Hürthle cells in a cellular smear.
5. The smear shows nuclear features which are suggestive of papillary carcinoma like nuclear grooving and ground glass nuclei.
6. The smear shows a small proportion of thyroid follicular cells with nuclear enlargement.
7. The smear shows an atypical lymphoid infiltrate.

## **FOLLICULAR NEOPLASM / SUSPICIOUS FOR A FOLLICULAR NEOPLASM**

### **DEFINITION**

This diagnostic lesion implies to an aspirate which is markedly cellular and composed of thyroid follicular cells mainly arranged in a predominant microfollicle pattern.<sup>[40,43]</sup>

### **CRITERIA**

There is a markedly cellular smear and the thyroid follicular cell are arranged as microfollicle pattern. The thyroid follicular cells are relatively uniform, in size and have moderate amounts of cytoplasm. The nuclei are uniformly round with slight hyperchromatism and no nucleoli.<sup>[44]</sup> The hallmark of this category is microfollicular pattern. The “microfollicle” pattern refers to the arrangement of follicular cells in flat groups with less than 15 cells per group and the cells are arranged in a circle that is at least two-thirds complete. The microfollicle sometimes may contain a small amount of colloid. The size of the microfollicles tend to be uniform. When the sample is sparsely cellular and the smear contains predominantly microfollicles, it is advisable to classify such lesions under the category of **ATYPIA OF UNDETERMINED SIGNIFICANCE** and the patients are managed according to the category. The parathyroid adenomas when

aspirated the smears show crowded and overlapping follicular cells which are uniform in size so they are often misinterpreted as **FN/SFN**.

### **FOLLICULAR NEOPLASM, HURTHLE CELL TYPE/ SUSPICIOUS FOR A FOLLICULAR NEOPLASM,HUTHLE CELL TYPE**

The Hürthle cell is also called Askanazy cell because its named after its discoverer and the other names of Hurthle cells include oxyphilic cell, and oncocyte, the Hurthle cell is defined as a thyroid follicular cell which is large in size with abundant granular cytoplasm and have enlarged round to oval nucleus with prominent nucleoli. These cells are commonly seen in some reactive or hyperplastic conditions like lymphocytic (Hashimoto's) thyroiditis (LT) and multinodular goiter (MNG) these cells are considered as metaplastic, non-neoplastic follicular cells in these conditions but the Hurthle cells can be seen in neoplastic conditions like (Hürthle cell adenoma and Hürthle cell carcinoma). <sup>[40,45,46]</sup>

### **DEFINITION**

This category comprises of a smear that is markedly cellular and consists predominantly of Hürthle cells.

### **CRITERIA**

The Hürthle cells in smear have abundant granular cytoplasm which stains pink with hematoxylin and eosin and the nucleus is large and may be central or eccentric in location with prominent nucleoli. The Hürthle cells are

predominantly seen as singly scattered cells, but sometimes these cells can also be seen in crowded clusters or in syncytial pattern.

There are three problematic features in diagnosing a minimum criteria of FNHCT/SFNHCT, these include

1. when the smear is sparsely cellular and is predominantly composed of Hürthle cells;
2. when the smeas is moderately-to-markedly cellular and exclusively composed of Hürthle cells without atypia;
3. An abnormal smear which shows partial or minimal Hürthle cell differentiation.

In a FNA procedure when the smear shows <75% of the large cells are Hürthle cells it should be classified as “Follicular Neoplasm/Suspicious for a Follicular Neoplasm” rather than the FNHCT/SFNHCT. [47,48]

The differential diagnosis of FNHCT/SFNHCT includes the neoplasms like Papillary carcinoma of thyroid, the HCNs may show papillary pattern of arrangement with characteristic nuclear features of papillary carcinoma and conversely the cells in classic papillary carcinomas of thyroid often show focal oncocytic differentiation. This feature is particularly seen in the oncocytic variant of papillary carcinoma [40,49]

Another differential diagnosis of HCNs is medullary carcinoma. The medullary carcinomas are composed of cells which have abundant amount of fine granular cytoplasm thus confusing with a Hürthle cell. The Hürthle cell

contains prominent nucleoli which is almost absent in most medullary carcinoma. On staining with Romanowsky stains, the cytoplasmic granules of Hürthle cells are stained blue in color whereas in medullary carcinoma the cytoplasmic granules are stained usually red.

In parathyroid adenomas the cells mimicks like the cells of HCNs but the arrangement of the cells in parathyroid adenomas in monomorphous pattern and the nuclei showing features of “salt and pepper” chromatin are not seen in HCN.<sup>[50]</sup>

## **SUSPICIOUS FOR MALIGNANCY**

### **DEFINITION**

This category of suspicious for malignancy (SFM) is reported when the smear shows strong features of malignancy (mainly papillary thyroid carcinoma ) but the cytological findings present in the smear are not definite to make a conclusive diagnosis of malignancy.<sup>[51]</sup> Such diagnostic category is created with the aim of acheiving a very high positive predictive value of the malignant lesions

### **CRITERIA**

#### **SUSPICIOUS FOR PAPILLARY CARCINOMA<sup>[52,53]</sup>**

##### **Pattern A (Patchy Nuclear Changes Pattern)**

In this pattern the smear is highly cellular. The pattern of arrangement is in macrofollicle clusters and some of the cells show characteristics nuclear

features of papillary carcinoma such as nuclear grooves, nuclear molding, and nuclear pseudoinclusion.

#### **Pattern B (Incomplete Nuclear Changes Pattern)<sup>[54]</sup>**

In this pattern the aspirate is of variable cellularity. The smear obtained can be sparsely cellular, moderately, or highly cellular. The nucleus shows features of papillary carcinoma but in an incomplete pattern, there is presence of mild nuclear atypia and pallor the nuclear grooves are seen but the characteristic intranuclear pseudoinclusions are not present.

#### **Pattern C (“Sparsely Cellular Specimen Pattern”)**

In this category the smear although it is sparsely cellular but it contains many features of papillary thyroid carcinoma.

#### **Pattern D (Cystic Degeneration Pattern)<sup>[59]</sup>**

This pattern shows features of cystic degeneration such as the presence of cystic macrophages laden with hemosiderin. The arrangement of thyroid follicular cells is seen mainly in clusters or in diffuse sheets and the individual cells have large pale nuclei and some of the nucleus shows nuclear grooves, but the intranuclear inclusions are absent and there is presence of occasional “histiocytoïd” type of cells which have enlarged nuclei and abundant vacuolated cytoplasm. <sup>[57,58,59]</sup>

## **SUSPICIOUS FOR MEDULLARY CARCINOMA**

The smear is sparsely cellular. The smear shows a uniform population of single dispersed small to medium sized cells. The nuclear cytoplasmic ratio is high and the nuclei is eccentrically located, and shows smudged chromatin and admixed in a background of amorphous material.

## **SUSPICIOUS FOR LYMPHOMA**

The smear can be cellular or sparsely cellular. When the sample is cellular it is composed of numerous population of monomorphous population of lymphocytes. When the smear is sparse in cellularity the atypical lymphocytes may be present.

## **SUSPICIOUS FOR MALIGNANCY, NOT OTHERWISE SPECIFIED**

The other thyroid malignancies which are encountered in thyroid if present can cause poor cellularity and thus a diagnosis of SFM is opted in such conditions.

## **PAPILLARY THYROID CARCINOMA AND ITS VARIANTS<sup>[60,61]</sup>**

The most common malignancy in thyroid is papillary thyroid carcinoma and it constitutes for about 70- 80% of all cancers seen in thyroid and is seen predominantly in females in the age group of 30's to 40s. External radiation to the neck during childhood presents as a risk factor for this malignancy. The clinical presentation is usually as a nodular lesion. Papillary thyroid carcinoma usually spreads via lymphatics to the lungs. The prognosis of papillary thyroid carcinoma is good. <sup>[53]</sup>



## **DEFINITION**

Papillary thyroid carcinoma is a malignant epithelial tumor which shows peculiar nuclear features. The pattern is papillary.<sup>[53]</sup>

## **CRITERIA**

The thyroid follicular cells are arranged in papillary pattern or as in diffuse sheet like pattern. The nuclear features of papillary carcinoma are very characteristic and mentioned below:

1. Nuclei are enlarged which can be oval or irregularly shaped with some nuclei may show molding.
2. Longitudinal nuclear grooves are present.
3. Intranuclear cytoplasmic pseudoinclusions.
4. The nuclei is pale (“Orphan Annie” nuclei).
5. The nucleoli is small and can be solitary or multiple.
6. Psammoma bodies are sometimes present.
7. Multinucleated giant cells are common.
8. The colloid is variable and may be stringy, ropy, or “bubble-gum”-like consistency.

## **VARIANTS OF PAPILLARY CARCINOMA<sup>[60,61]</sup>**

### **DEFINITION**

These lesions have the characteristic nuclear features of Papillary thyroid carcinoma but architectural pattern is different, the prescence of

colloid and its consistency and there is a lymphoplasmacytic infiltrate in the background of the smear which can be prominent if present or it can be absent.

## **FOLLICULAR VARIANT OF PAPILLARY CARCINOMA**

### **DEFINITION**

This variant is the most common variant of papillary carcinoma and is composed of thyroid follicles which are small to medium-sized and have peculiar nuclear features of papillary carcinoma of thyroid. There is a predominant microfollicle type of arrangement in the smear and sometimes the smear may be composed of normal sized follicles. And if in this variant the smear is composed predominantly of macrofollicle clusters it is considered as a different entity. [63,64]

### **CRITERIA**

Smears are hypercellular, with arrangement of thyroid follicular cells in syncytial sheets and in microfollicles. Some thick colloid may be present within the neoplastic follicle. The nuclear changes are subtle.

## **MACROFOLLICULAR VARIANT OF PAPILLARY CARCINOMA<sup>[65,66]</sup>**

### **DEFINITION**

This variant of papillary thyroid carcinoma contains thyroid follicles arranged predominantly in macrofollicle clusters.

## **CRITERIA**

The smear consists of diffuse sheets of variably sized follicles. The nuclear features are essential for a conclusive evidence of malignancy. The background of the smear shows lot of thin or thick colloid. The differential diagnosis of this variant includes the nodular goiter in a benign follicular nodule and the follicular adenoma of the macrofollicular type<sup>[66,67]</sup>

## **CYSTIC VARIANT OF PAPILLARY CARCINOMA<sup>[68]</sup>**

### **DEFINITION**

This variant is predominantly cystic and composed of thin cystic fluid, with abundant macrophages.<sup>[57]</sup>

## **CRITERIA**

The thyroid follicular cells are seen as sheets, papillae, or follicles. Tumor cells are “histiocytoid” in appearance with hemosiderin laden macrophages admixed with thin colloid. The nuclear characteristics of papillary carcinoma are essential for a conclusive diagnosis of this malignancy .

## **ONCOCYTIC VARIANT OF PAPILLARY CARCINOMA<sup>[70]</sup>**

### **DEFINITION**

In this category the follicular cells have characteristic nuclear features of papillary carcinoma and are seen admixed with a prominent population of oncocytic cells. The oncocytic cells are round to oval with abundant granular eosinophilic cytoplasm.

## **CRITERIA**

In this category the smear shows a predominant population of oncocyctic cells which are commonly arranged in papillary pattern or in diffuse sheets or as single cells but the nuclear peculiarity of papillary thyroid carcinoma are mandatory for a conclusive evidence of this variant.

[70,71]

## **WARTHIN LIKE VARIANT OF PAPILLARY CARCINOMA<sup>[72]</sup>**

### **DEFINITION**

This category presents as a circumscribed thyroid neoplasm with a papillary pattern of arrangement and usually admixed with lymphoid follicles that mimics the Warthin tumor of parotid gland.

## **CRITERIA**

The follicles are arranged in papillary pattern and composed predominantly of thyroid follicular cells which are predominantly oncocyctic and also some of the cells are present as singly dispersed cells admixed in a lymphoplasmacytic background. The nuclear characteristics of papillary thyroid carcinoma are a must for a conclusive evidence.

## **TALL CELL VARIANT OF PAPILLARY CARCINOMA<sup>[73,74]</sup>**

### **DEFINITION**

This variant is an aggressive form of papillary thyroid carcinoma and is composed of thyroid follicular cells arranged in papillary pattern the individual thyroid follicular cells are elongated and arranged in single layer

which have abundant cytoplasm which is dense and granular and contains the characteristic nuclear features of papillary thyroid carcinoma.

### **CRITERIA**

Tall cells with abundant cytoplasm should be present in more than 50% of the tumor mass to allow it to be classified as a tall cell variant of papillary carcinoma with characteristic nuclear features are present for a definite diagnosis of this variant. The chromatin is more granular with few psammoma bodies and intranuclear inclusions are more frequently present.

### **COLUMNAR CELL VARIANT OF PAPILLARY CARCINOMA <sup>[75]</sup>**

#### **DEFINITION**

This variant is aggressive and is composed predominantly of columnar cells which have cytoplasmic vacuoles which can be supranuclear or subnuclear. The neoplastic cells are commonly seen as papillary pattern, but trabecular and follicular arrangement can also be seen.

### **CRITERIA**

Aspirates are cellular and there is no colloid in the background. The tumor cells are arranged in papillary pattern, in groups, and diffuse sheets, and sometimes seen as small tubules. There is elongation and stratification of nuclei. And as a rule the characteristic nuclear features of papillary thyroid carcinoma are a must to conclude a conclusive evidence.

## **HYALINIZING TRABECULAR TUMOR<sup>[76]</sup>.**

### **DEFINITION**

This tumor shows the thyroid follicular cells arranged in trabeculae and there is hyalinization in between the trabeculae growth and most important feature is that it contains the nuclear peculiarities of papillary thyroid carcinoma.

### **CRITERIA**

The tumor cells are arranged around a hyaline stromal material. The nuclear features like intranuclear inclusions and nuclear grooving are present.

There is a confusion regarding considering this tumor as a variant of papillary thyroid carcinoma or as a form of follicular adenoma. Because of its nuclear features, these tumors are mostly interpreted as papillary thyroid carcinoma or “suspicious for papillary thyroid carcinoma.”<sup>[77]</sup>

## **MEDULLARY THYROID CARCINOMA**

Medullary thyroid carcinoma constitutes of about 7% of thyroid malignancy. There are two forms of appearance in this tumor sporadic and heritable forms. The heritable forms include the multiple endocrine neoplasia (MEN) type 2A (Sipple’s syndrome), which includes mainly pheochromocytomas and hyperparathyroidism in some families; MEN type 2B (mucosal neuroma syndrome or Gorlin’s syndrome), which mostly

includes mucosal neuromas and with somatic marfanoid habitus; and admixed with familial medullary thyroid carcinoma (FMTC).<sup>[78]</sup>

## **DEFINITION**

It is a malignant neoplasm and is derived from the parafollicular cells of the thyroid gland.

## **CRITERIA OF MTC**

The aspirates are moderate to markedly cellular. The thyroid follicular cells are single cells alternating with cells in syncytial clusters. The individual tumor cells are plasmacytoid, polygonal, round, and/or spindle-shaped. And a mild nuclear pleomorphism is usually seen. The nuclei are often round and the chromatin can be fine or coarsely granular (“salt and pepper”) chromatin. Occasionally the pseudoinclusions in nucleus are present and often the nucleus can be binucleated and multinucleated. There is inconspicuous nucleoli but sometimes it can be prominent also. The cytoplasm is granular and variable. The amyloid is often present in the smear and is seen as a dense, amorphous material. There is strongly immunoreactivity in tumor cells for calcitonin, CEA, chromogranin, synaptophysin, and TTF-1, and are negative for thyroglobulin.<sup>[78,79]</sup>

The most common differential diagnosis of medullary thyroid carcinoma is a Hürthle cell neoplasm but papillary carcinoma, anaplastic carcinoma, hyalinizing trabecular tumor plasmacytoma, and metastatic tumors like melanoma also warrant consideration in some instances.

Immunohistochemistry markers help in differentiation between these tumors.<sup>[79]</sup>

## **POORLY DIFFERENTIATED CARCINOMA**

### **DEFINITION**

In this category the thyroid follicular cells are arranged in insular, solid, or trabecular growth pattern. The pure form of poorly differentiated carcinoma lacks the characteristic nuclear features of papillary thyroid carcinoma but has peculiar features like mitoses, necrosis, or small convoluted nuclei. The most classic pattern of poorly differentiated thyroid carcinoma is the insular type of arrangement which is shown by cells arranged in nests or groups and shows a outlining of thin fibrovascular core. In a few cases poorly differentiated thyroid carcinoma can be seen admixed with well differentiated thyroid carcinoma like follicular carcinoma, papillary carcinoma.<sup>[80]</sup>

### **CRITERIA**

The smears are cellular and shows a insular, solid, or trabecular pattern. The thyroid follicular cells are uniform with scant cytoplasm with occasional plasmacytoid appearance. The individual tumor cells show nuclear atypia which is variable.<sup>[81]</sup>

## **UNDIFFERENTIATED (ANAPLASTIC) THYROID CARCINOMA**

This variant of thyroid carcinoma is also called as “giant and spindle cell carcinoma,” it is an aggressive thyroid malignancy which is extreme in



nature and accounts for less than 5% of thyroid malignancy. Prognosis is poor compared to other thyroid malignancy and there is a female predominance. There is a hard, nodular thyroid gland, and most of the patients presents with a rapidly growing mass. There is marked tumor growth which leads to neck enlargement and may present with or without reactive fibrosis, and this may infiltrate into surrounding soft tissues of the neck.<sup>[82]</sup>

## **DEFINITION**

Undifferentiated thyroid carcinoma is a high grade thyroid malignancy that is pleomorphic and composed of epitheloid and spindle cell features.

## **CRITERIA**

Smears are variably cellular but there is usually marked cellularity. The tumor cells are arranged as single cells or in clusters. The tumor cells are epitheloid or spindle-shaped and they range in various sizes. The tumor cells can be plasmacytoid. The nuclei of the tumor cells show mild pleomorphism with some of the nucleus shows parachromatin clearing, with prominent irregular nucleoli, with some intranuclear inclusions, and in some cases the nucleus can be eccentrically placed, and often admixed with multinucleation. Background shows necrosis and there is extensive inflammation which is predominantly composed of neutrophils. In some cases the osteoclast-like giant cells may be present. The mitotic figures are increased in count and often numerous and abnormal.<sup>[82]</sup>

## **SQUAMOUS CELL CARCINOMA OF THYROID**

This thyroid cancer accounts for less than 1% of all thyroid cancers. Like undifferentiated thyroid carcinoma, it usually occurs in elderly and has a poor prognosis.

### **DEFINITION**

This diagnostic category includes a malignant tumor in thyroid that shows exclusively squamous differentiation.

### **CRITERIA**

The smears in this category are almost exclusively composed of large, pleomorphic keratinized cells admixed with few areas showing necrosis.

### **METASTATIC TUMORS IN THYROID**

The metastatic tumors in thyroid are very rare. It is important to recognize these lesions in fine needle aspiration smears of thyroid nodules. In some cases metastasis to the thyroid can be the initial presentation of a distant tumor. Tumors of the nearby organs like pharynx, larynx, esophagus, mediastinum, and the nearby lymph nodes can also involve the thyroid. The thyroid is most commonly metastasized in cancers of the lung, breast, skin and kidney. The metastatic carcinomas to thyroid can manifest as three patterns (1) they can present as multiple small discrete nodules (less than 2 mm); (2) or they can present as solitary large nodules; and (3) or can involve as a diffuse involvement.

## **1. METASTATIC RENAL CELL CARCINOMA**

A majority of these lesions present as solitary or multiple nodules and the lesions from metastatic renal cell carcinomas are of clear cell type and they can occur after a long gap of even 20 years following the removal of the primary cancer in the patient.<sup>[82]</sup>

### **DEFINITION**

The metastatic renal cell carcinoma is a malignant tumor that is seen arising from any one of the kidneys and subsequently involves the thyroid gland.

### **CRITERIA**

The aspirates are markedly cellular. The tumor cells are arranged in small clusters, fragmented papillae in sheets or can be seen as single dispersed cells. The individual tumor cells have abundant granular, clear or vacuolated cytoplasm. The nuclei are round to oval with prominent nucleoli. The aspirates are haemorrhagic.<sup>[82,83]</sup>

## **2. METASTATIC MALIGNANT MELANOMA<sup>[84]</sup>**

It is a malignancy that is derived from the cells which are differentiating towards melanocytes that arises from the skin or, can arise from the extra-cutaneous sites and thus involves the thyroid gland.

### **CRITERIA**

The smears are moderately cellular and most of the cells are noncohesive. The cells can be plasmacytoid, spindle shaped, and can present

as anaplastic forms. The nuclei are large and are often eccentrically placed. Sometimes intranuclear cytoplasmic pseudoinclusions can be seen. The cells are immunoreactive for S-100 protein, melanA, and HMB45.<sup>[84]</sup>

## **METASTATIC ADENOCARCINOMA FROM BREAST**

### **DEFINITION**

It is an epithelial type of malignancy arising from the cells differentiating towards the ductal epithelium and involves the thyroid gland.

### **CRITERIA**

The aspirates are moderately cellular and composed of monomorphous cells. The cells can be seen in single or in small clusters.

## **METASTATIC PULMONARY CARCINOMA**

The smears from the bronchogenic carcinomas depends on the nature of primary tumor. The metastatic small cell carcinoma resembles the insular pattern of the thyroid carcinoma. The individual tumor cells in tumors like adenocarcinomas of pulmonary origin are composed of medium-sized to large sized cells that are seen in diffuse form or can be seen in clusters. The cells are columnar in appearance with round to oval and eccentric nuclei and with prominent nucleoli.

## **MALIGNANT LYMPHOMA IN THYROID**

The Malignant lymphomas in thyroid can arise as a primary tumor or it can arise as a secondary as a manifestation of a systemic disease. Most of the primary thyroid lymphomas are of the B-cell type. The Lymphomas

constitutes about 5% of the thyroid neoplasms. Plasma cell malignancy in thyroid and Hodgkin lymphoma are rare malignancy in thyroid.<sup>[85,86]</sup>

### **EXTRANODAL MARZINAL ZONE B-CELL LYMPHOMA**

Aspirates are markedly cellular and there is prescence of lymphoid cells in clusters or as singly scattered. The individual cells are small in size and are about twice as bigger as that of a small lymphocyte. The individual tumor cells have moderate amount of cytoplasm vesicular nuclei and have open chromatin and nucleoli are present which are small. Another population of large cells are seen which have eccentric nuclei, coarse chromatin, and prominent nucleoli. These cells are often seen along with centrocytes, the monocytoïd B-cells, and plasma cells. Sometimes the follicular and oncocytiç type of thyroid epithelial cells are seen along with lymphoid cells<sup>[85]</sup>

### **DIFFUSE LARGE CELL LYMPHOMA**

The samples are cellular and there is often seen many lymphoglandular bodies in the background. The aspirates usually contain uniform and singly scattered large lymphoid cells. The nucleus shows coarse chromatin shows one to two prominent nucleoli.<sup>[87]</sup>

**THE BETHESDA SYSTEM FOR REPORTING CYTOPATHOLOGY:  
IMPLIED RISK OF MALIGNANCY AND RECOMMENDED  
CLINICAL MANAGEMENT**

*[TABLE -3] : Risk of malignancy in different categories in Bethesda and proper management.*

<b>Diagnostic Category</b>	<b>Risk of malignancy(%)</b>	<b>Usual management</b>
Non- diagnostic or unsatisfactory	-	Repeat FNA with ultrasound guidance
Benign	0-3	Clinical follow up
Atypia of undetermined significance / Follicular lesion of undetermined significance	5-15	Repeat FNA
Follicular neoplasm / Suspicious for follicular neoplasm	15-30	Surgical lobectomy
Suspicious for malignancy	60—75	Near –total thyroidectomy
Malignant	97-99	Total thyroidectomy

The TABLE-3 shows the risk of malignancy in each category of Bethesda and proper clinical management in each category. By classifying the thyroid lesions in these categories avoids the confusion in management of patients and thus helps in uniform communication among different clinicians and helps in proper patient management. In ND/UNS category, patients are managed by a repeat thyroid FNA which is done 3months later to avoid the false positive interpretation due to reparative change. In Benign category ,the patients are managed by regular follow up at 6-18 months interval for a period of 3-5 years. In AUS category the patients are managed by a repeat FNA after an appropriate interval and the mostly correlated clinically and the risk of malignancy is close to 5-15%.In FN/SFN category the patients are usually managed by surgery which is usually a hemithyroidectomy or a lobectomy and the risk of malignancy is close to 15-30%. In SFM category the patients are usually managed by a near – total thyroidectomy as the risk of malignancy is higher in this category and is almost close to 60-75%. In Malignant category the patients are usually managed by a total thyroidectomy as the risk of malignancy is almost 97-99% .

## **MATERIALS AND METHODS**

### **ETHICAL CONSIDERATION**

The study was conducted after obtaining approval from the Institutional Ethical Committee of Tirunelveli Medical College, Tirunelveli. This prospective study was carried out in the Cytopathology Laboratory of the Department of Pathology Tirunelveli Medical College, Tirunelveli from January 2013 to June 2014. All the patients who reported to the department of pathology with a requisition to perform FNAC with clinically detectable thyroid swelling were included in the study.

A total of 300 cases was included in the study. The patients referred from Surgical OPD, Medicine OPD, ENT and other OPDs was included in the study.

A detailed clinical history was taken and recorded on a proforma with special emphasis on thyroid function.

A detailed general examination was also carried out. Examination of the thyroid done as per the standard protocol and recorded in the proforma. Fine needle aspiration was carried out in the cytopathology laboratory.

### **INCLUSION CRITERIA**

All patients who presented with thyroid swelling irrespective of age and sex.

### **EXCLUSION CRITERIA**

The patients who had not given a written informed consent.



## **PROCEDURE**

All patients were seen and informed written consent was obtained from each patient prior to FNAC.

After obtaining the consent and giving a brief explanation about the procedure to the patient, aspiration was done with the patient in supine or sitting position with hyperextended neck, so as to make the thyroid swelling prominent.

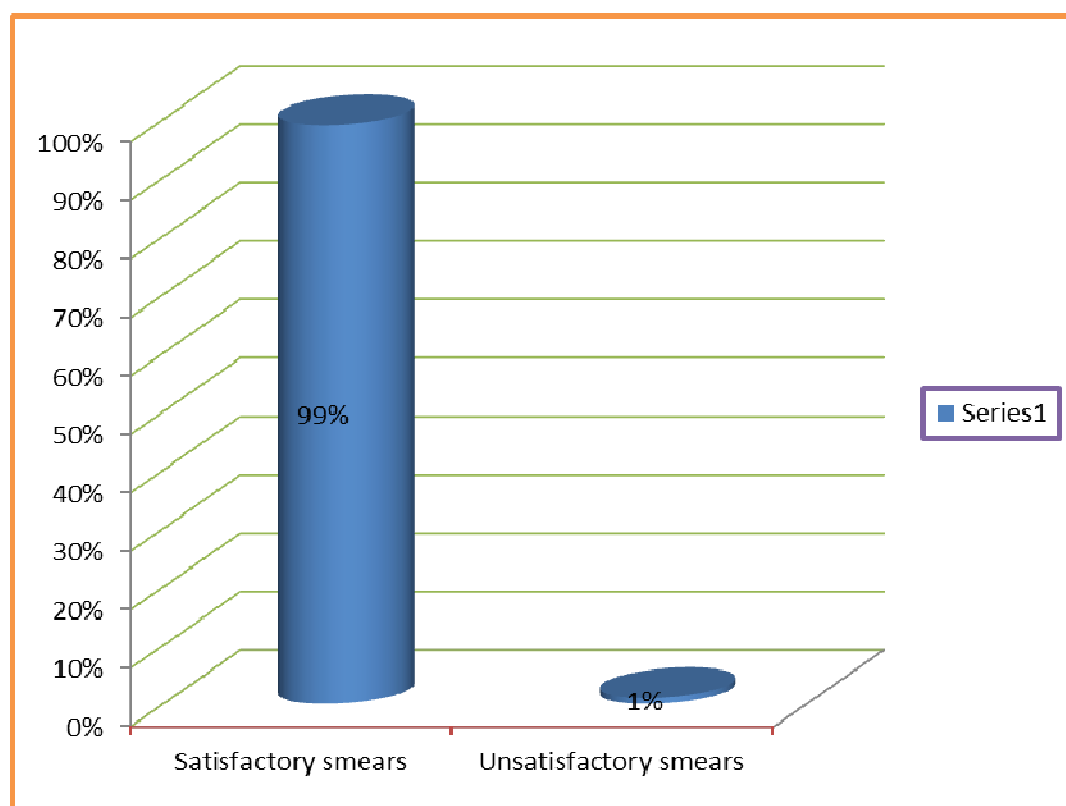
Under aseptic precautions a 23 gauge needle with syringe was inserted into the lesion. Three to four to and fro movements were performed quickly. Under negative pressure, material gets collected in the needle. After collection of material, negative pressure was released, needle with syringe holder was removed. The material was spread over clean labelled slides and smears were prepared and stained by Hematoxylin and Eosin method(H&E). Whenever fluid was aspirated the whole content was aspirated and centrifuged and smears then made with the sediment and stained with H&E. In such cases whenever a residual mass was observed, it was reaspirated. In case of multiple nodules, more than one aspirate was done from prominent nodules. No serious complication occurred in our study.

The cytopathology report was then given according to the standard reporting format as suggested by the Bethesda system for reporting thyroid cytopathology.

## OBSERVATION AND RESULTS

### STUDY DESIGN [CHART-1]

FNAC was done on 300 patients with the history of thyroid swellings during a period from January 2013 to June 2014. Of the 300 aspirations, 297 aspirates were satisfactory smears and 3 smears were unsatisfactory.[CHART-1]



***CHART- 1 : Percentage of satisfactory and unsatisfactory smears in present study***

## **AGE OF DISTRIBUTION [TABLE-4], [CHART -2]**

In this study it was noted that the maximum clustering of cases occurred in the age group from second to and fourth decade of life (68%) between the age group of 20- 49 years.

In this study the youngest patient with thyroid lesion was a 9 year old female and oldest one was a 85 years old female. The mean age is 38.3 years with a standard deviation of 14.917.

It was noted that 2 cases presented with thyroid lesions in the age group of 0-9 years and both were benign lesions.

The highest percentage of cases occurred in the age group of 30-39 years.

The age group of 20-29 yrs and 40-49 years had similar percentage of distribution of cases in this study. The remaining age groups had average number of cases. In the age group of > 70 years, 11 cases were present out of the total 300 cases in this study.

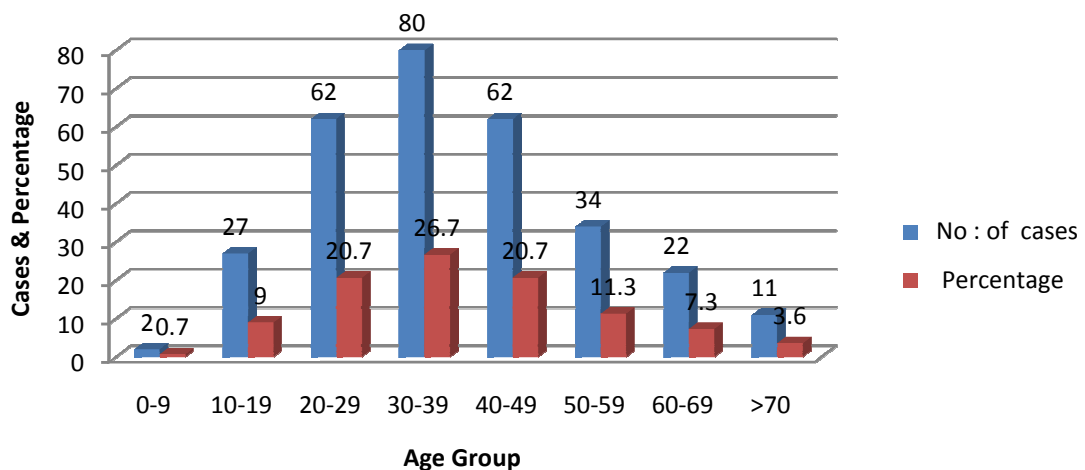
The incidence of benign lesions (69.6%) were most commonly seen from second to fourth decade of life and malignant lesions most commonly occurred in the seventh decade of life (37.5%).

## AGE WISE DISTRIBUTION OF THYROID LESIONS

**TABLE -4 : Total no of cases and percentage according to age group**

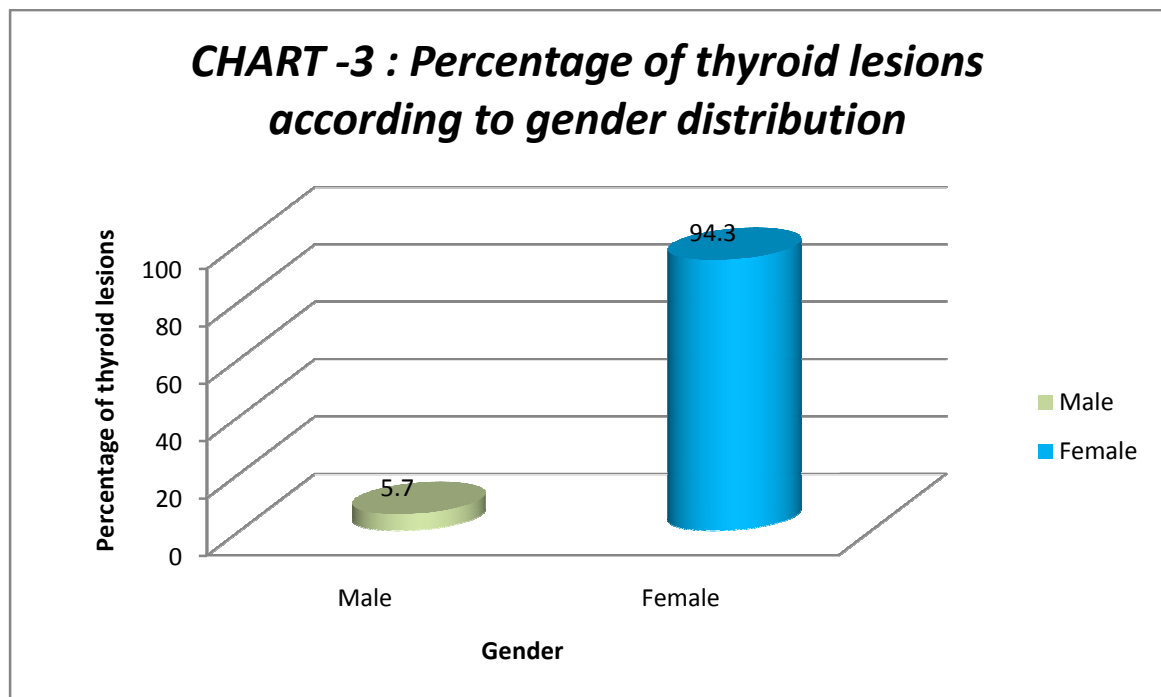
Age (in years)	No : of cases	Percentage
0-9	2	0.7
10-19	27	9
20-29	62	20.7
30-39	80	26.7
40-49	62	20.7
50-59	34	11.3
60-69	22	7.3
>70	11	3.6
<b>TOTAL</b>	<b>300</b>	<b>100</b>

**CHART 2 : No of thyroid lesions in different age group**



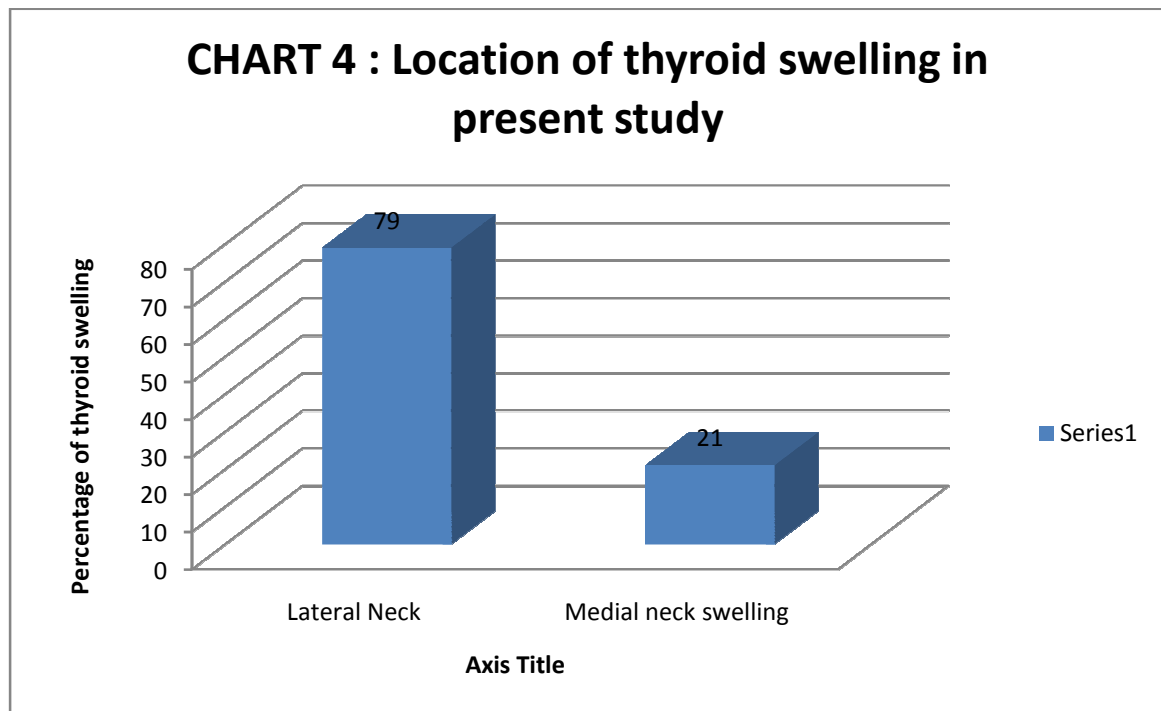
### **GENDER DISTRIBUTION [ CHART- 3]**

Among the 300 cases who presented with thyroid swelling in this study the majority of cases were females (94.3%) and the males comprised of (5.7%) and the female : male ratio was 16.5: 1.



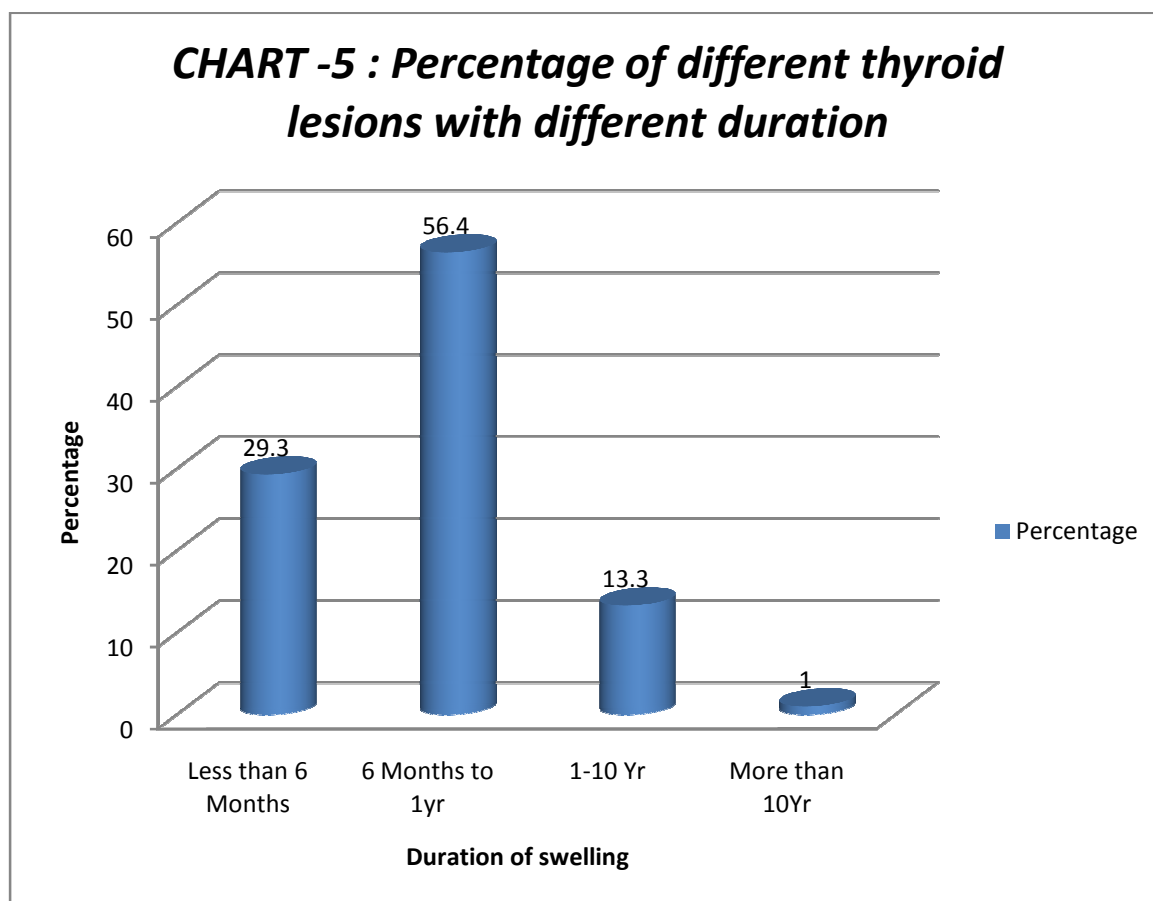
### **CLINICAL PRESENTATION [CHART -4]**

Out of the 300 cases who presented with thyroid swelling in this study most of the patients presented with lateral neck swelling (79%) of thyroid whereas rest of them presented as a midline swelling (21%) in thyroid which is depicted in CHART-4, mentioned below.



#### **DURATION OF SWELLING [CHART -5]**

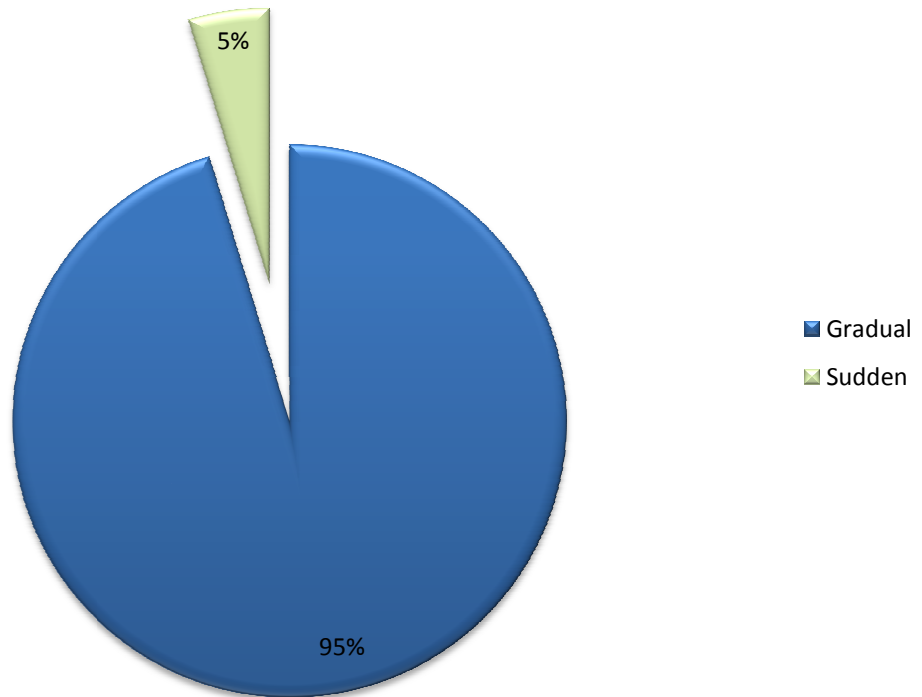
Out of 300 cases, who presented with thyroid swelling, the duration of swelling was noted it was < 6 months in 29.3% of cases, 6 months to 1 year in 56.3% of cases, 1- 10 years in 13.3% cases and > 10 years in 1% of cases. Maximum number of cases presented with a duration of 6 months to one year which is depicted in the CHART -5 mentioned below.



### **RATE OF GROWTH [CHART-6]**

Out of 300 cases who presented with swelling of thyroid in this study it was noted that 95.3% of patients had gradual progression of disease and 4.7% had a sudden progression of disease. Most of the individuals in this study presented with a history of gradual onset of increase in size of the swelling.

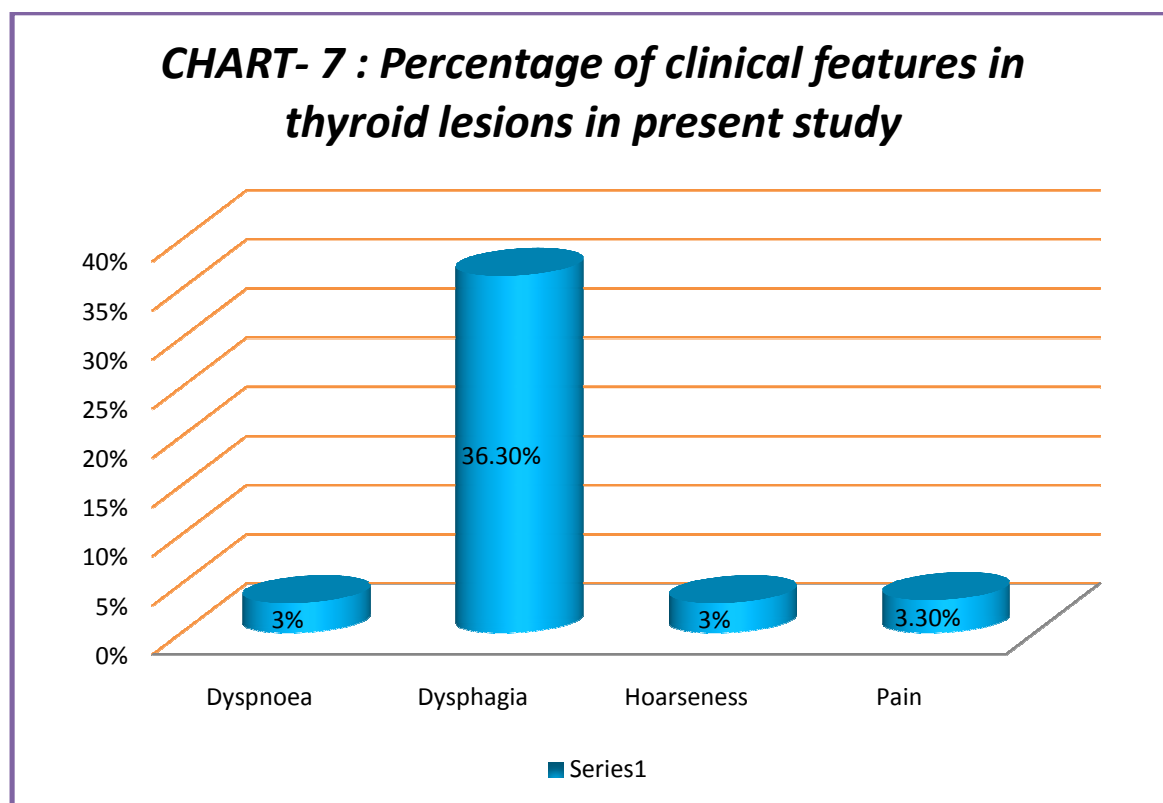
***CHART -6 : Percentage of thyroid lesions showing rate of growth***



### **CLINICAL SYMPTOMS [CHART -7]**

Out of the total 300 cases who presented with the thyroid swellings in this study, it was noted that the most common clinical symptoms was dysphagia in 26.39% of patients followed by dyspnoea in 3% of cases, hoarseness of voice in 3% of patients and pain in 3.3% of patients and the rest of the patients presented with no significant complaints. Most of the individuals who presented in this study had no significant complaints.





## **FUNCTIONAL STATUS OF THE THYROID SWELLING [CHART-8]**

Out of the total 300 cases studied, majority of the patients were euthyroid.

### **I.HYPOTHYROID FEATURES**

Out of 300 cases, 12.3% cases presented with features of hypothyroidism like bradycardia and dry skin.

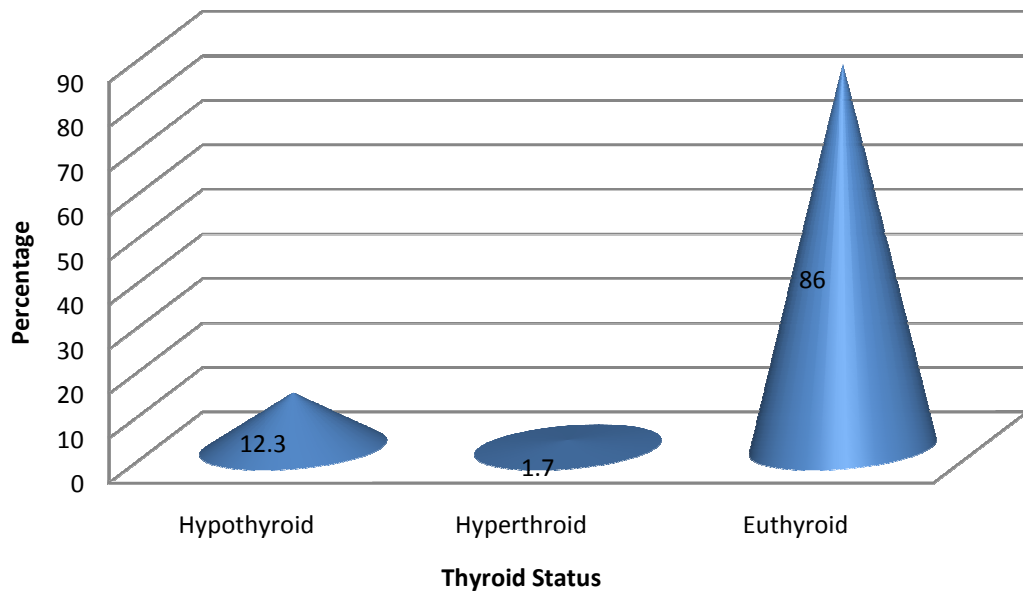
### **II.HYPERTHYROID FEATURES**

Out of the total 300 cases, 1.7% cases presented with features of hyperthyroidism which were tachycardia and moist skin.

### **III. EUTHYROID**

Out of the total 300 cases, 86% cases were euthyroid and had no significant complaints.

***CHART 8: Percentage of functional status of thyroid lesions in present study***



## **HORMONAL LEVEL ESTIMATION**

### **T3, T4 and TSH LEVELS**

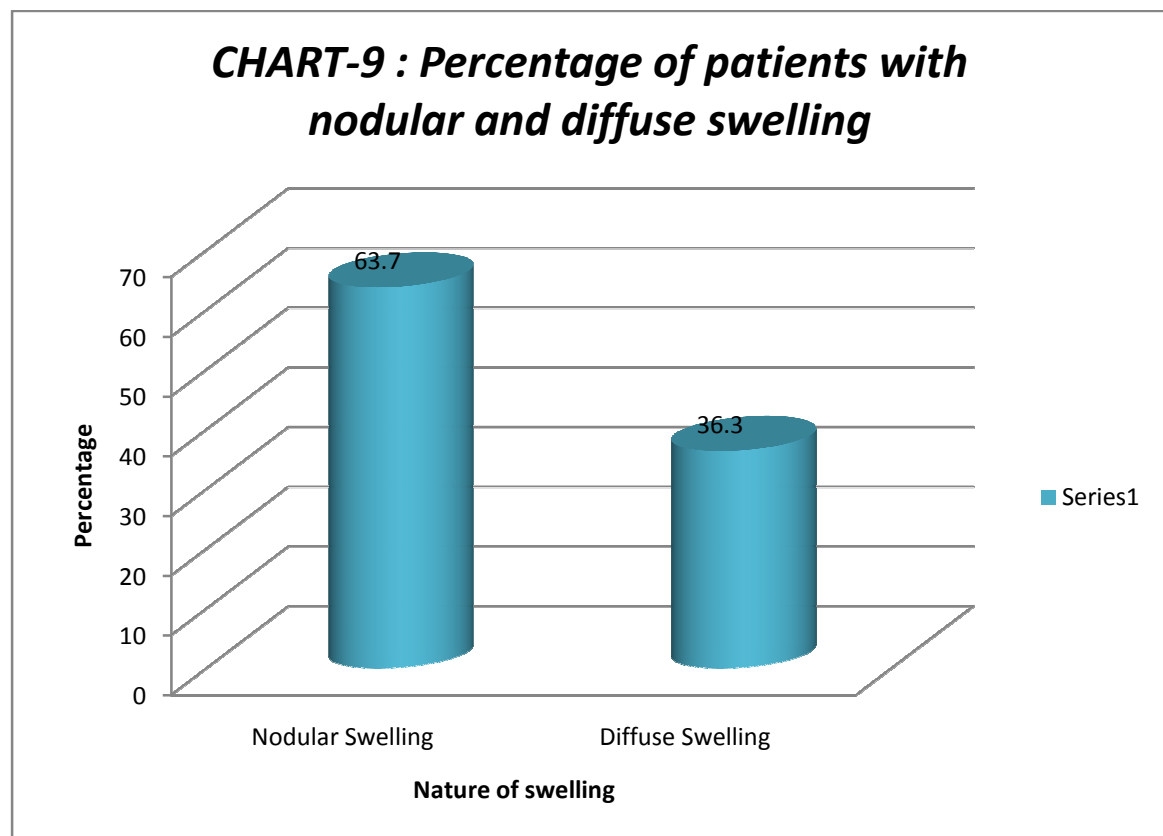
Among the 37 patients who presented with features of hypothyroidism clinically 35 cases (94.6%) had decreased T3, T4 levels and increase in TSH levels. These patients presented with clinical symptoms of hypothyroidism like bradycardia and dry skin.

Among the 5 patients who presented with features of hyperthyroidism clinically, 4 cases (80%) had increased T3 and T4 levels and all of them had decreased TSH levels and all of these patients presented with clinical symptoms of hyperthyroidism like tachycardia and moist skin.

Majority of the individuals who presented with thyroid swelling in our study were euthyroid and as such had no significant complaints and their hormonal levels were in the normal range.

### **NATURE OF THYROID SWELLING [CHART-9]**

Of the total 300 cases who presented with thyroid swelling in our study, 191 cases (63.7%) presented with features of nodular swelling, and 109 cases (36.3%) presented with features of diffuse swelling and out of the 191 cases of nodular swelling 159 cases (83.2%) had solitary nodule and 32 cases (16.8%) presented with multiple nodules. Majority of the patients presented with a nodular swelling of thyroid and which was mostly solitary in nature.



## **CORRELATION OF MICROSCOPING FINDINGS WITH NATURE OF THYROID SWELLING**

Of the total 300 cases who presented with thyroid swelling in this study , 159 cases (53%) presented with solitary nodule, 32 cases (10.7%) presented with multiple nodules, and the remaining 109 cases (36.3%) presented with diffuse swelling of thyroid.

### **SOLITARY NODULE – 159 (53%) [CHART-10]**

Cystic lesion	-	3
Benign	-	140
Follicular neoplasm	-	9
Papillary carcinoma	-	7

### **MULTIPLE NODULE - 32 (10.6%) [CHART -11]**

Benign	-	28
Follicular neoplasm	-	3
Neoplastic	-	1
Cystic	-	0

### **DIFFUSE SWELLING - 109(36.3%)**

Benign	-	40
Hashimoto's thyroiditis	-	69

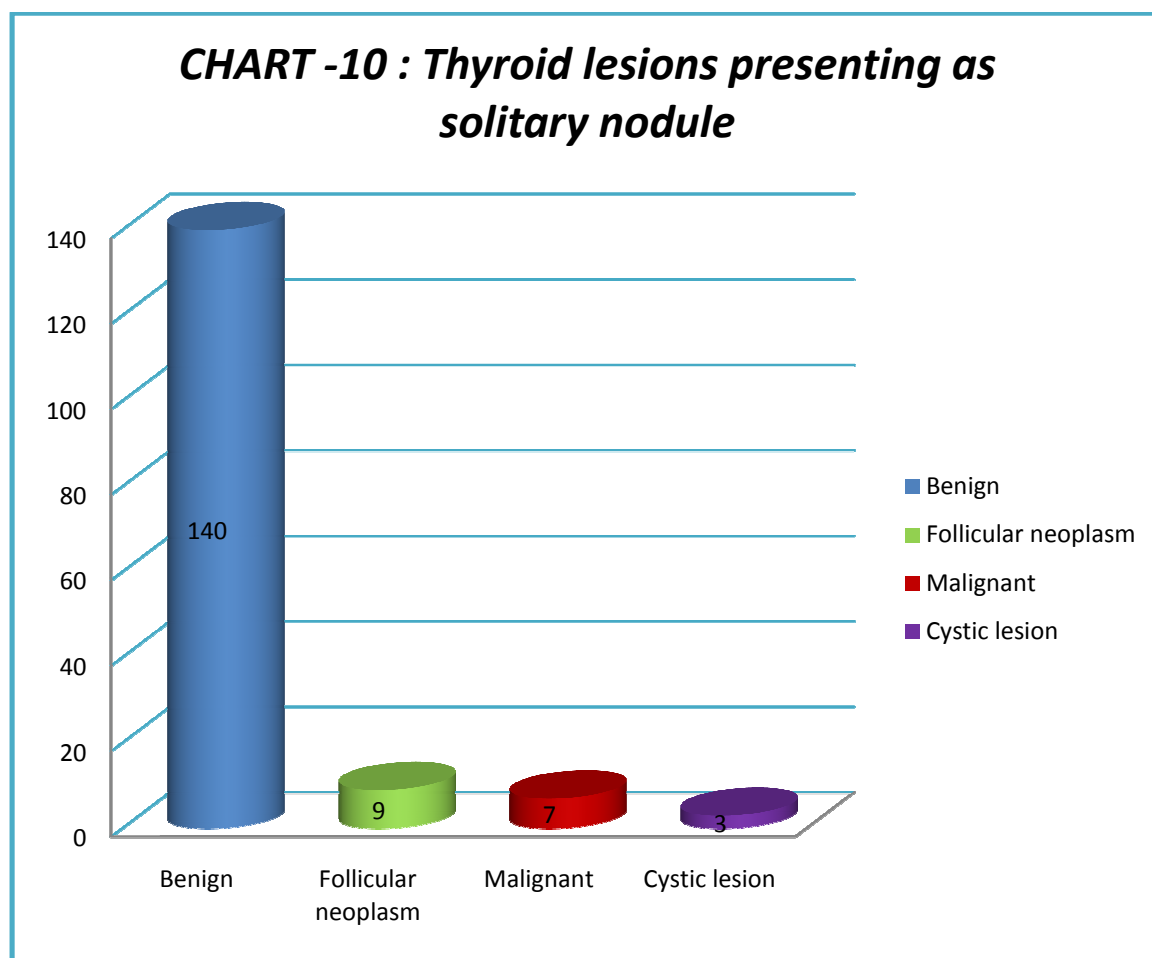
Of the total 300 cases, the cystic lesion was present in 3 cases and all of them presented as solitary nodules, the benign lesion was reported in 277 cases. Out of the 300 cases 159 cases presented as solitary nodules and out of

the 159 cases 140 cases (88%) were reported as benign, 9 cases (5.7%) reported as follicular neoplasm, 7 cases (4.4%) were reported as malignant and 3 cases (1.9%) were reported as cystic lesion. Out of the 300 cases 32 cases presented as multiple nodules and out of the 32 cases benign lesion was reported in 28 cases (87.5%), 3 cases (9.3%) were reported as follicular neoplasm and 1 case (3.1%) was reported as malignant. Out of the 300 cases, 109 cases presented as diffuse swelling. Out of the 300 cases follicular neoplasm was reported in 12 cases out of which 9 cases (75%) presented as solitary nodules 3 cases (25%) presented with multiple nodules. Out of the total 300 cases 8 cases of papillary carcinoma diagnosed in this study, 7 cases (87.5%) presented as solitary nodules and one case (12.5%) presented as multinodular swelling.

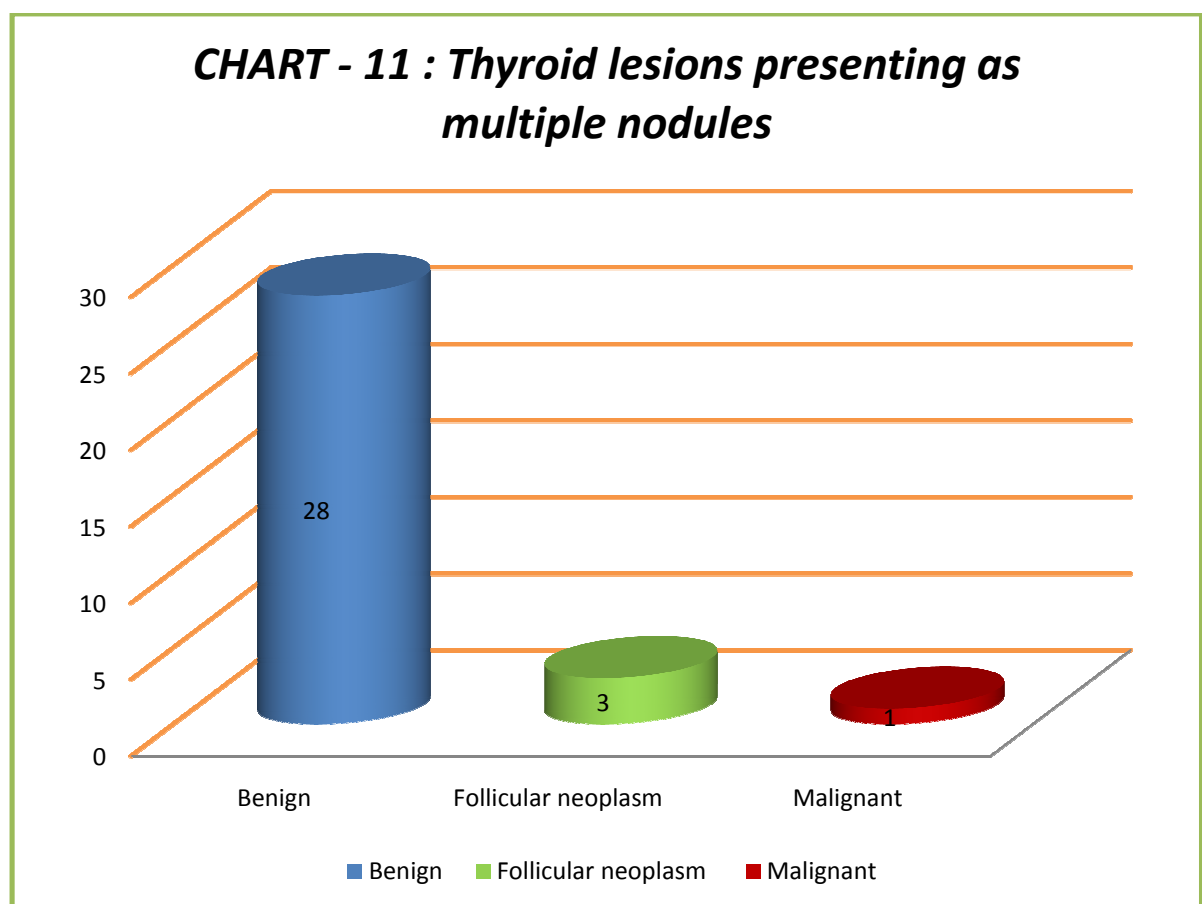
***TABLE-5: Correlation of microscopic findings with nature of the thyroid swelling***

<b>Nature of swelling</b>	<b>Cyst</b>	<b>Benign</b>	<b>Follicular Neoplasm</b>	<b>Papillary</b>	<b>Total</b>
<b>Solitary nodule</b>	3	140	9	7	159
<b>Multiple nodule</b>	0	28	3	1	32
<b>Diffuse swelling</b>	0	109	0	0	109
<b>Column totals</b>	3	277	12	8	300

The TABLE-5 shows the correlation of the microscopic findings with the nature of the thyroid swelling. It was noted that out of the 300 cases maximum cases 277 (92.3%) were reported as benign, 12 cases (4%) out of 300 were reported as follicular neoplasm, 3 cases (1%) out of 300 were reported as cystic lesion and 8 cases (2.7%) out of 300 were reported as malignant. Out of the 277 cases reported as benign, maximum cases, 140 cases (50.5%) presented as solitary nodules, 28 cases (10.1%) presented as multiple nodules and 109 cases (39.3%) presented as a diffuse swelling of thyroid.



The CHART -10 shows the percentage of thyroid lesions presented with solitary nodules and categorized in different microscopic criteria. Out of the total 300 cases 159 cases (53%) presented with solitary nodules. Out of 159 cases 3 cases (1.9%) diagnosed as cystic lesion, 140 cases (88%) as Benign lesions, Follicular neoplasm reported in 9 cases (5.7%) and Papillary carcinoma in 7 cases (4.4%).



The CHART -11 shows the percentage of thyroid lesions presented with multiple nodules. Out of the total 300 cases, 32 cases presented as multiple nodules. Out of the 32 cases presented as multiple nodules benign lesion was reported in 28 cases (87.5%), Follicular neoplasm in 3 cases

(9.4%) and Papillary carcinoma in 1 case (3.1%) and no case presented with cystic lesion.

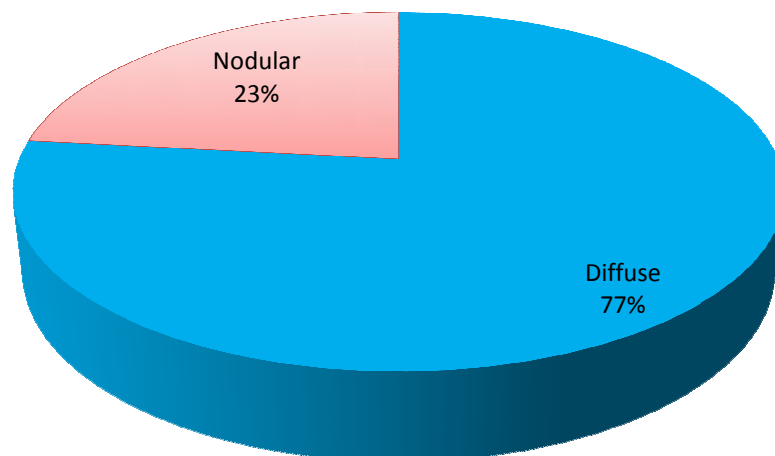
## **NATURE OF SWELLING IN HASHIMOTO'S THYROIDITIS**

### **[CHART-12]**

Out of the total 300 cases, who presented with a thyroid swelling in this study, 90 patients were diagnosed as Hashimoto's thyroiditis and out of the 90 cases 69 cases presented with a diffuse swelling in thyroid and the remaining 21 cases presented with a nodular swelling.

In this study most of the patients (76.7 %) with Hashimoto's thyroiditis presented with a diffuse swelling of thyroid and (23.3%) of cases presented with a nodular swelling of thyroid.

***CHART- 12 :Percentage of nodular and diffuse lesions in Hashimoto's thyroiditis.***

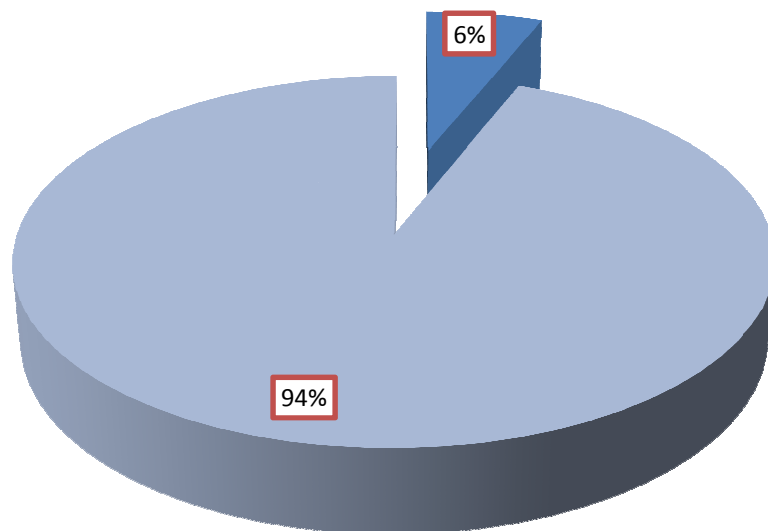




### SIZE OF THE SWELLING [CHART -13]

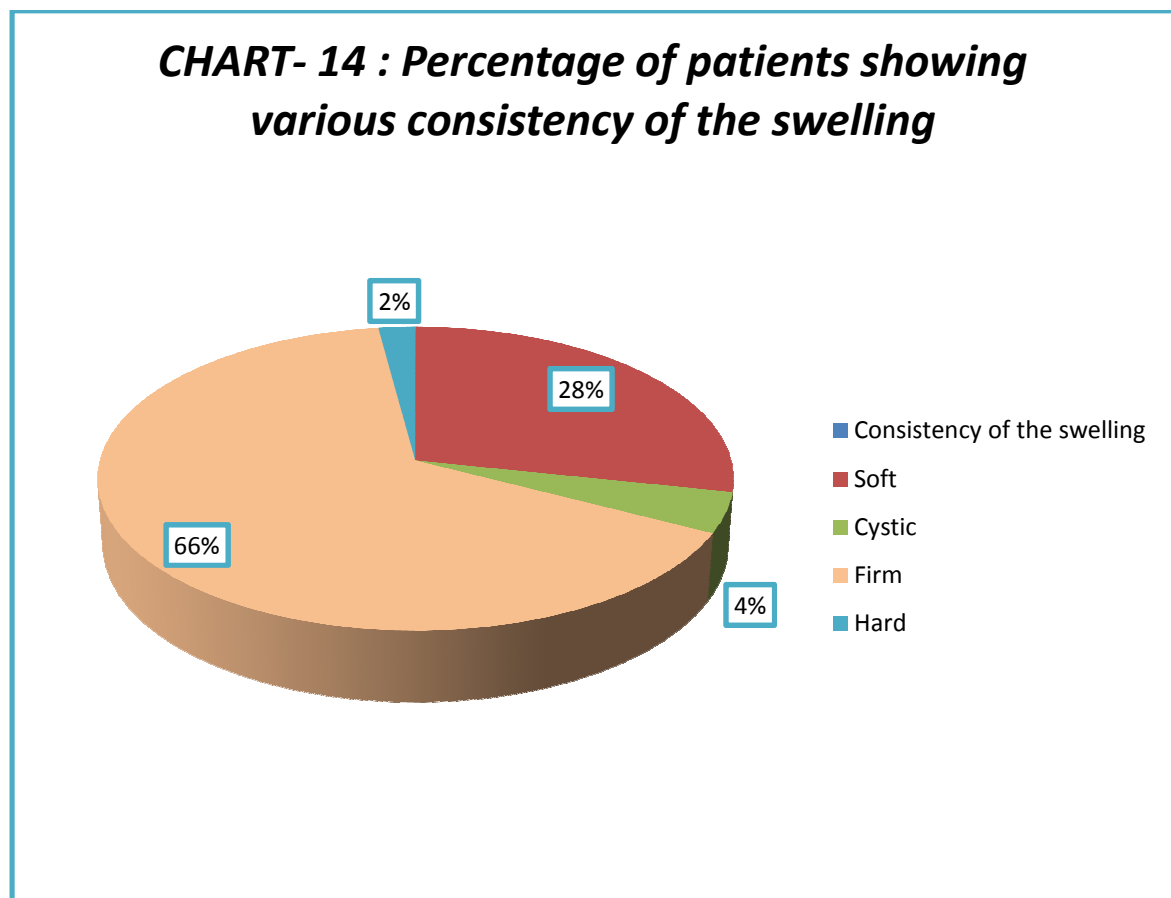
Of the total 300 cases who presented with thyroid swelling in our study, the size of the thyroid swelling was noted. Majority of the thyroid swelling were more than 1 cm. Out of the total 300 cases who presented in our study, 18 cases (6%) presented with a thyroid swelling of less than 1 cm and the rest 282 cases (94%) presented with thyroid swelling of more than 1 cm. All the thyroid swelling which were of size of less than 1cm, all of them were reported as benign lesion in thyroid.

**CHART- 13 : Percentage of size of swelling < or > 1 cm.**



## CONSISTENCY OF THE SWELLING [CHART -14]

Of the total 300 cases who presented with thyroid swelling the swelling was firm in consistency in 65.3% of patients, soft in consistency in 28.3% of patients and cystic consistency in 4.3% of patients and hard in consistency in 2.1% of patients.



## MOVEMENT WITH DEGLUTITION

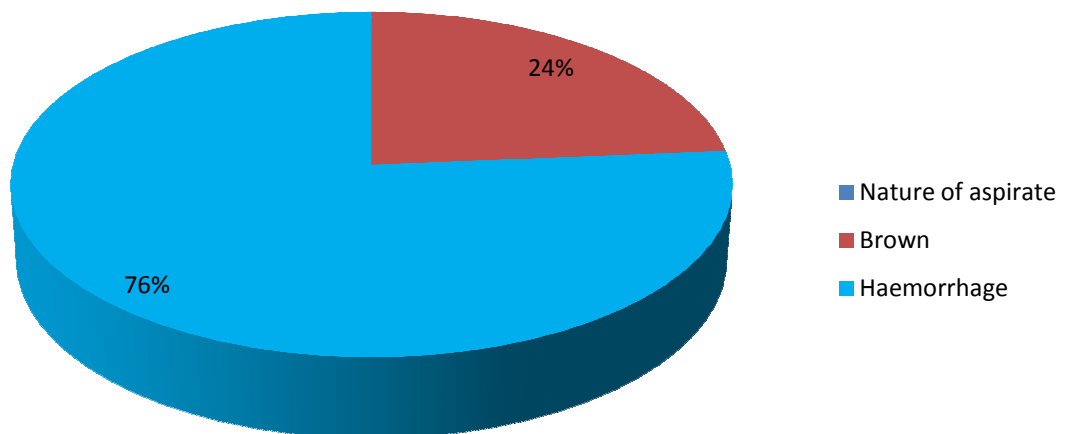
Of the total 300 cases presented with thyroid swelling in our study most of the swellings moved with deglutition 292 (97.3%) of patients except in (2.7% ) of patients it did not moved with deglutition.

## NATURE OF THE THYROID ASPIRATE [CHART- 15]

Of the total 300 cases presented with thyroid swelling, the aspiration was done in all 300 cases of which 71 cases (23.7% ) had a brown color aspirate and the rest of the cases 229 (76.3%) had a haemorrhagic aspirate.

Majority of follicular neoplasm (91.7%) and all the malignant lesions presented with a haemorrhagic aspirate.

***CHART- 15: Percentage of patients showing different nature of aspirate***

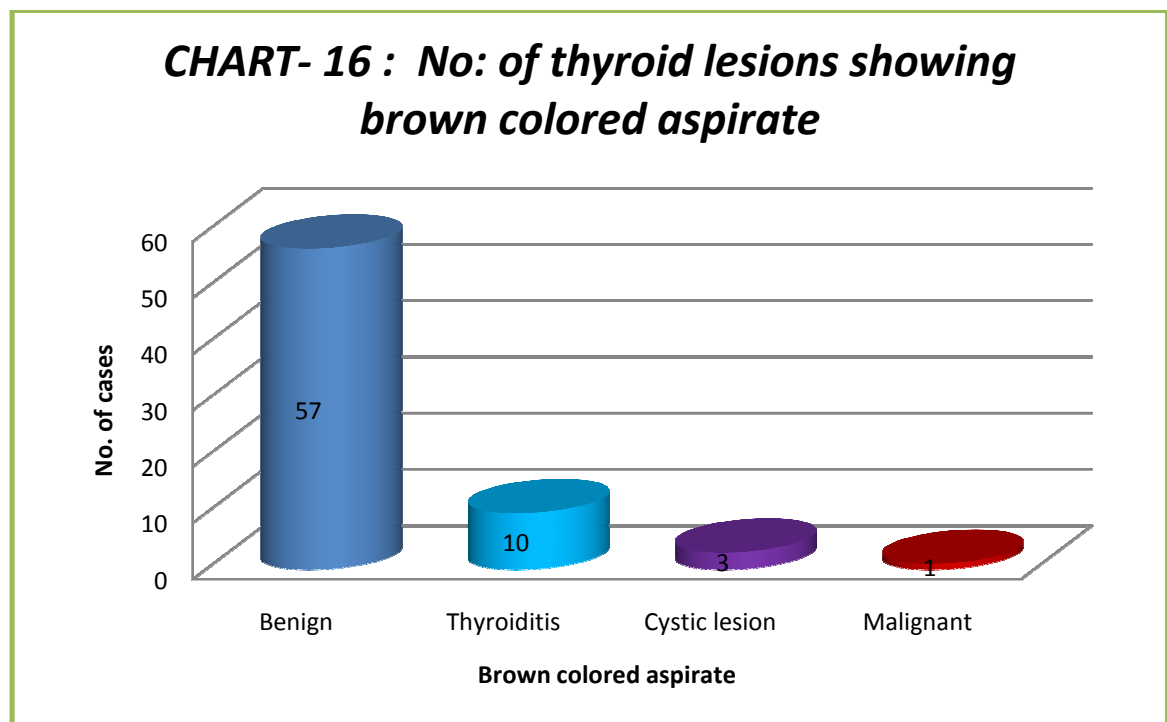


## ANALYSIS OF THE ASPIRATE

The analysis of aspirate from all 300 thyroid swelling was done and the aspirate was compared with the microscopic nature of the swelling and categorized as mentioned in CHART-16 and CHART-17.

### **BROWN COLOURED – 71 (23.7% ) [CHART -16]**

Cystic lesion	-	3
Benign	-	57
Thyroiditis	-	10
Malignant	-	1



The CHART-16 shows the thyroid lesions that showed a brown colored aspirate. Out of the 300 cases 71 cases (23.7%) presented with a brown color aspirate and out of the 71 cases the aspirate was reported as benign in 57 cases (80.3%), 10 cases (14.1%) were reported as thyroiditis,

3cases (4.2%) were reported as cystic lesion,1case (1.4%) was reported as malignant.

### **HAEMORRHAGIC ASPIRATE -229 (76.3% ) [CHART-17]**

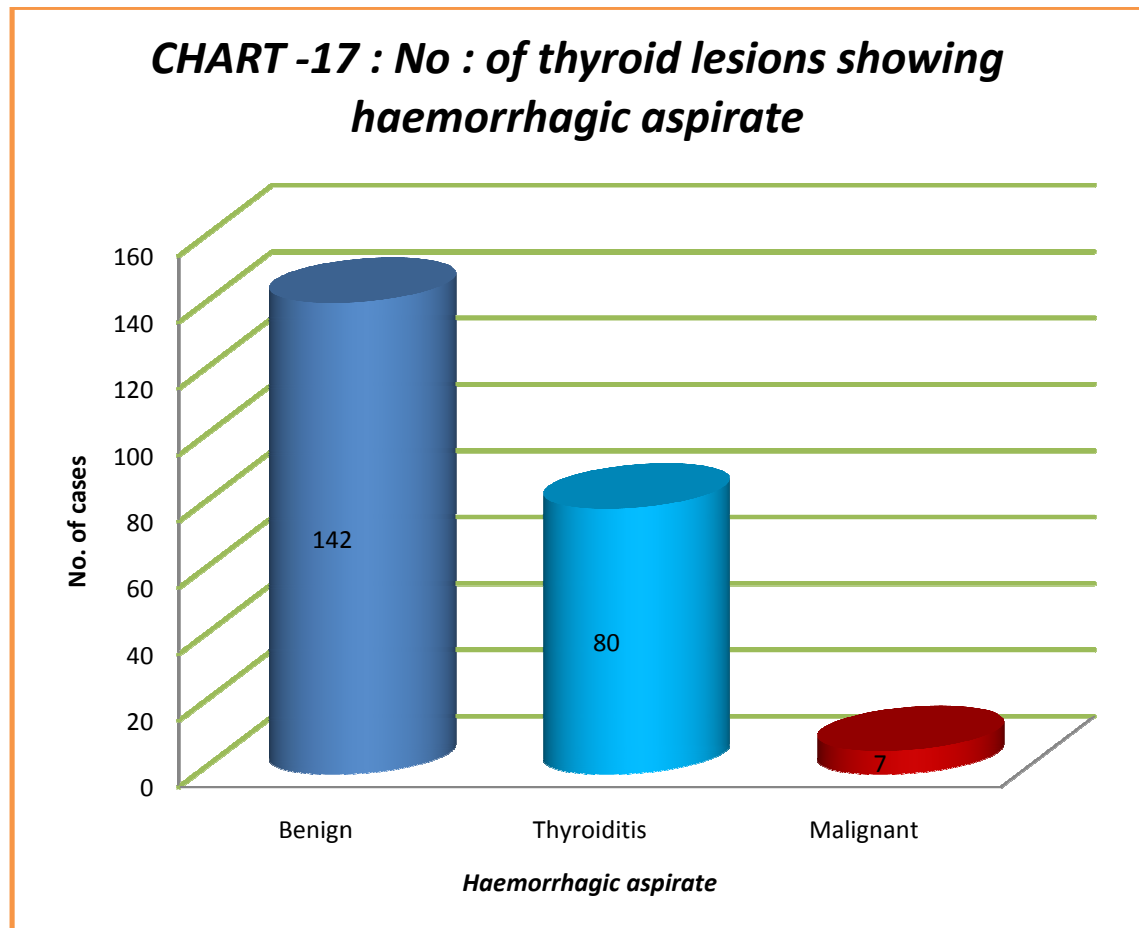
Cystic lesion - 0

Benign - 142

Thyroiditis - 80

Malignant - 7

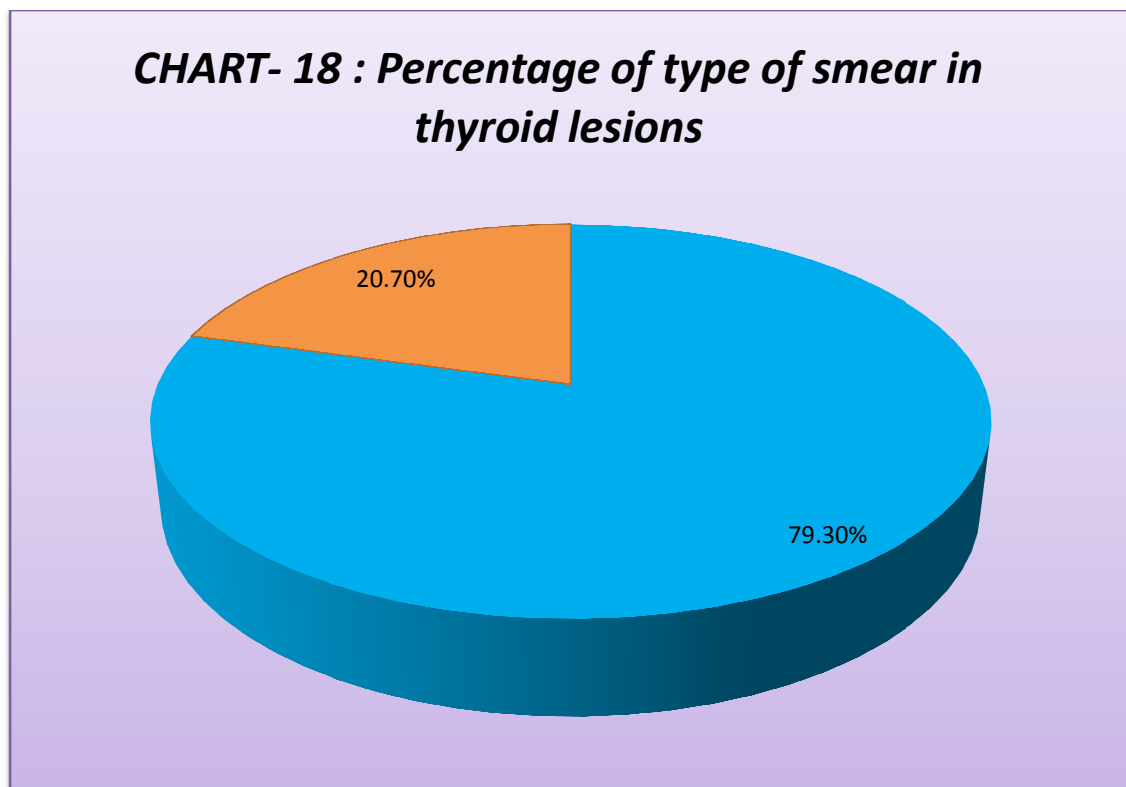
### ***HAEMORRHAGIC ASPIRATE***



The CHART-17 shows the thyroid lesions that showed a haemorrhagic aspirate. Out of the 300 cases 229 cases (76.3%) presented with a haemorrhagic aspirate and out of the 229 cases the aspirate was reported as benign in 142 cases (62%), 80 cases (35%) were reported as thyroiditis, 7 cases (3%) was reported as malignant.

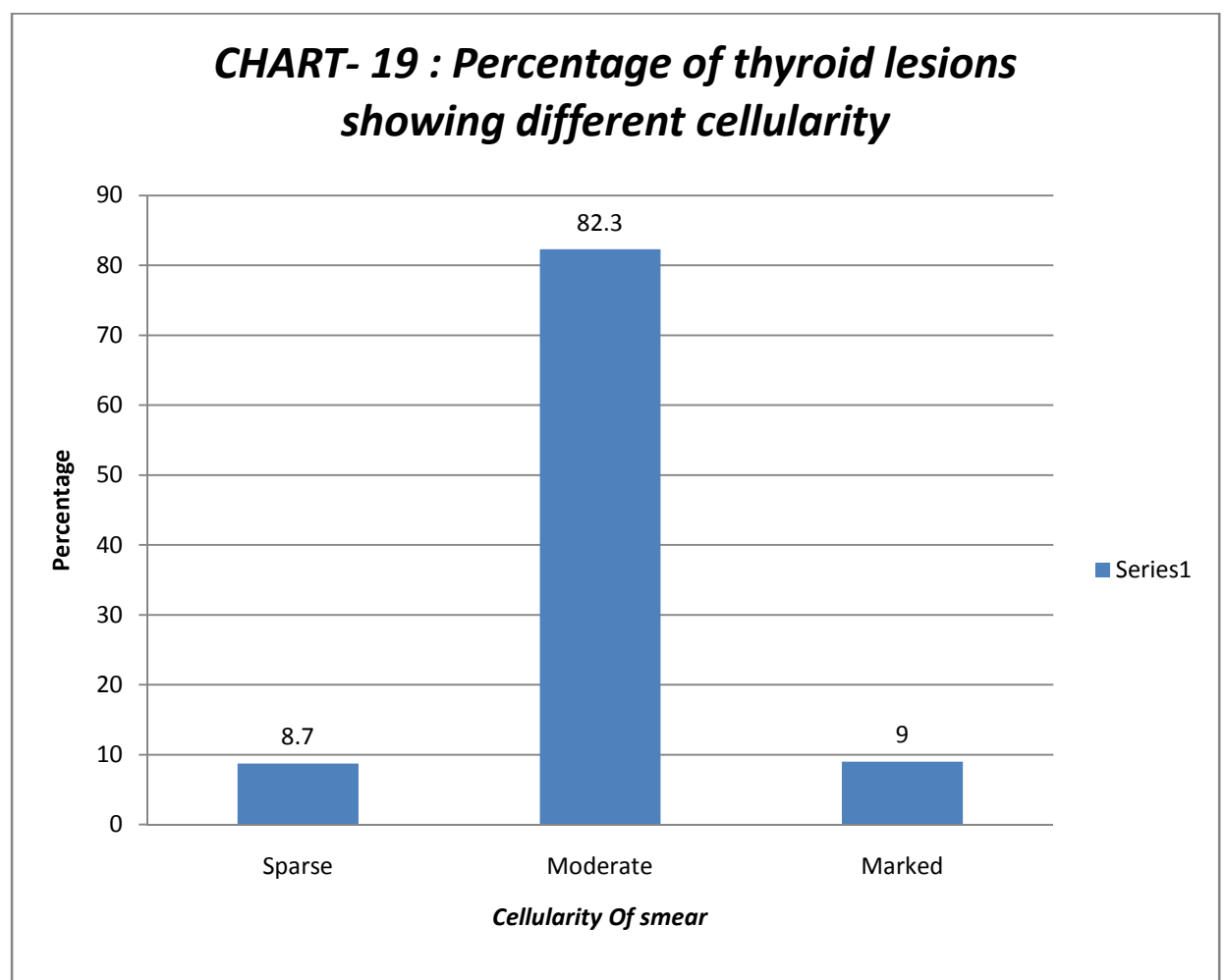
#### **TYPE OF SMEAR [CHART -18]**

Of the total 300 cases who presented with thyroid swelling the smear was directly made in 238 cases (79.3%) and it was a centrifuged smear in 20.7% of cases.



## CELLULARITY OF THE SMEAR [CHART- 19]

Of the total 300 cases the aspirations were sparse in cellularity in 26 cases (8.7%), moderate cellularity in 247 cases (82.3% ) and marked cellularity in 27 cases (9%). Out of the total aspirations the background of the smear showed colloid in 19% of cases and haemorrhage in 66.3% of cases and inflammatory background in 14.7% of cases.



**CYTOLOGICAL DIAGNOSES IN THYROID LESIONS BY  
CONVENTIONAL METHOD [TABLE – 6], [CHART- 20],[CHART-  
21]**

Out of the total 300 cases, 292 cases were diagnosed as benign by conventional cytological method and 8 cases were reported as malignant by the conventional method. Of the total aspirations diagnosed as benign, the colloid nodule was reported in 52 cases (17.3%), Nodular goiter in 108 cases (36%), Adenomatous goiter in 23 cases (7.7%), Hashimoto thyroiditis in 90 cases (30%), Follicular neoplasm in 12 cases (4%), Caseating granulomatous inflammatory pathology in 1 case (0.3%), cystic lesion of thyroid in 3 cases (1%), follicular neoplasm / dominant nodule of nodular goiter in 3 cases (1%). Of the total aspirations diagnosed as malignant, all of them were reported as papillary carcinoma of thyroid.

***TABLE - 6: Cytologic diagnosis in thyroid lesions by conventional method.***

**BENIGN LESIONS**

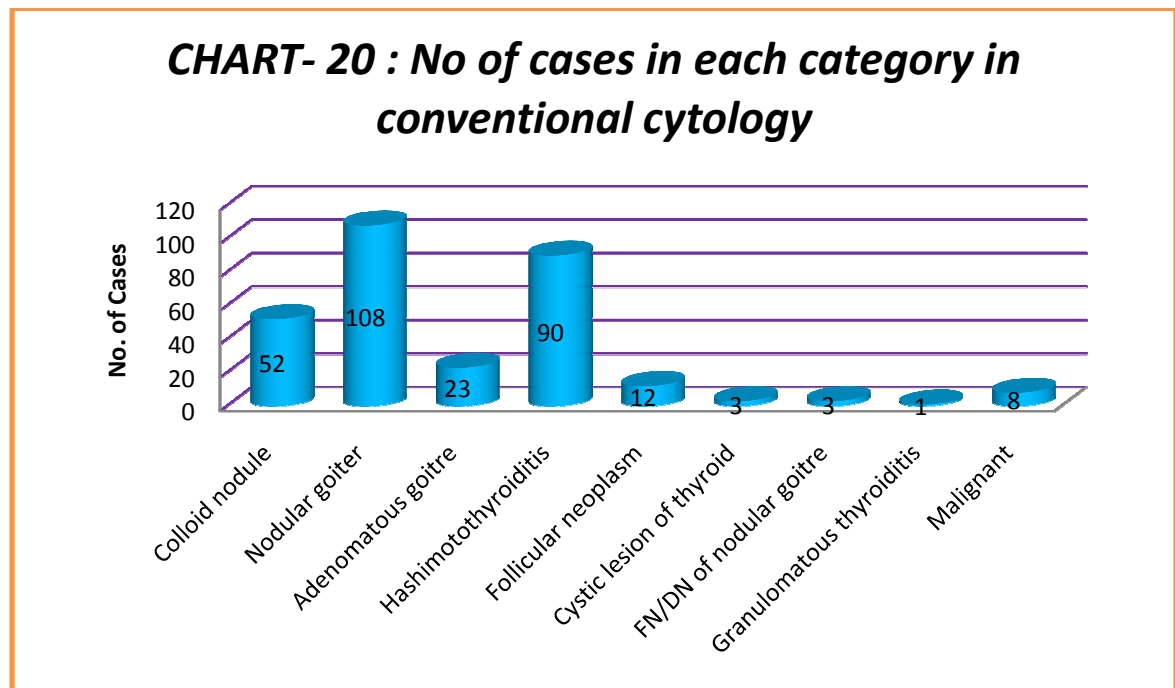
<b>Colloid nodule</b>	<b>Nodular goiter</b>	<b>Adenomatous goiter</b>	<b>Hashimoto thyroiditis</b>	<b>Follicular neoplasm</b>	<b>Cystic lesion of thyroid</b>	<b>FN/DN Of nodular goitre</b>	<b>Granulomatous thyroiditis</b>
52 (17.3%)	108(36%)	23(7.7%)	90(30%)	12(4%)	3(1%)	3(1%)	1(0.3%)

**MALIGNANT**

Papillary carcinoma – 8(2.7%)

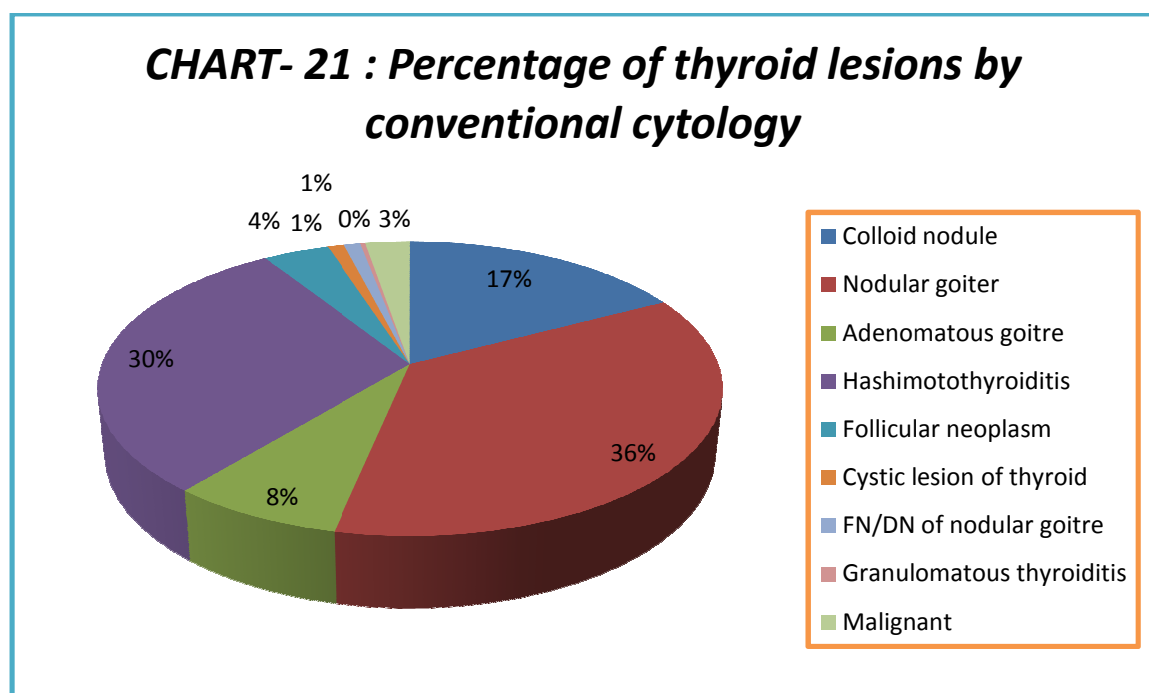


## CYTOLOGICAL DIAGNOSIS [CHART-20]



The CHART- 20 and CHART – 21 shows out of 300 cases diagnosed by conventional cytology a large number of cases were reported as nodular goitre, followed by Hashimoto's and colloid nodule.

## CYTOLOGICAL DIAGNOSES AS PER PERCENTAGE [CHART-21]



**AGE WISE DISTRIBUTION OF THYROID LESIONS ACCORDING TO CONVENTIONAL CYTOLOGICAL METHOD [TABLE-7],[CHART-22]**

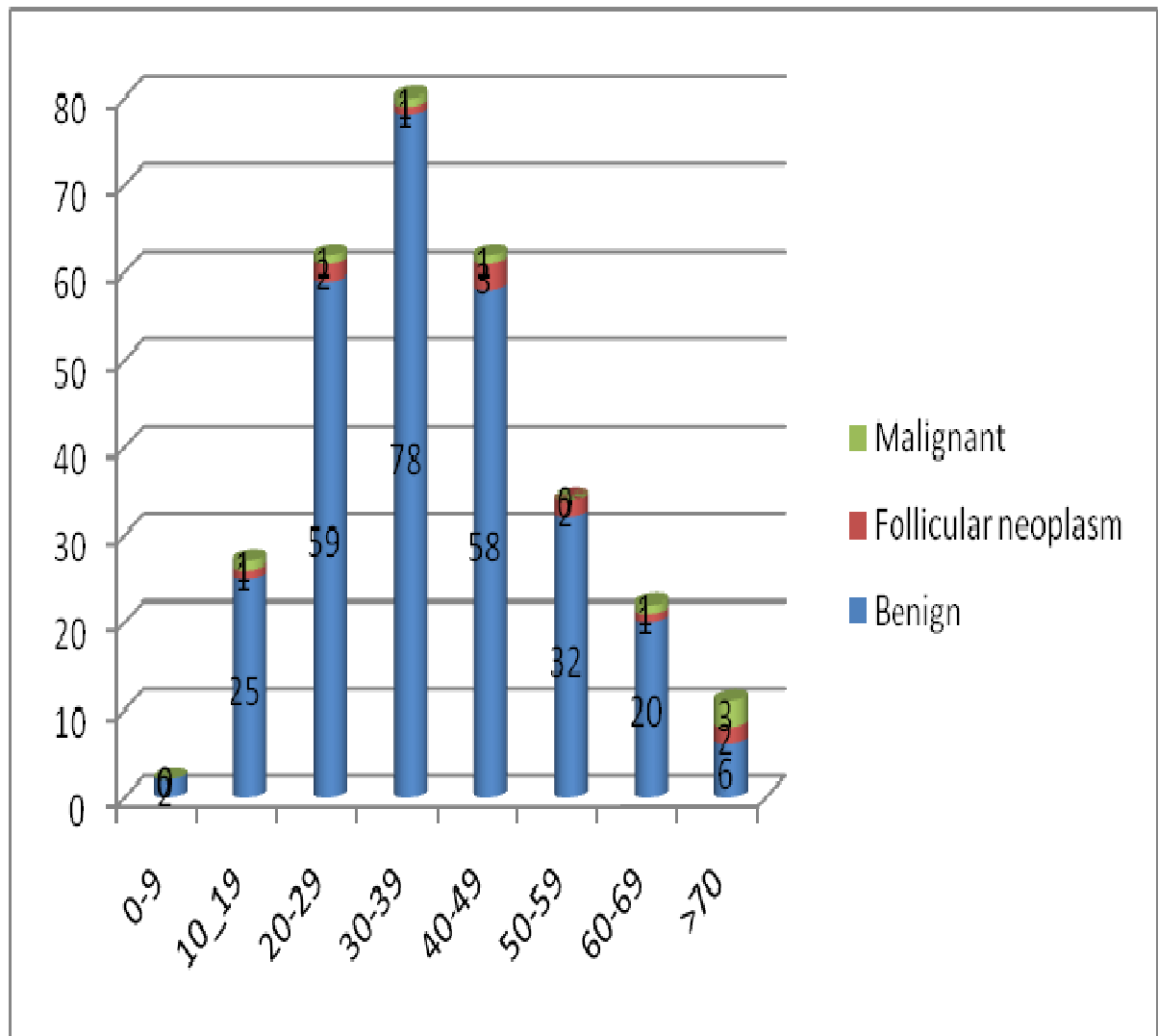
***TABLE- 7 : Age distribution of different thyroid lesions in present study according to conventional cytology.***

<b>Age (in years)</b>	<b>Benign</b>	<b>Follicular neoplasm</b>	<b>Malignant</b>	<b>Total</b>
0-9	2	0	0	2
10-19	25	1	1	27
20-29	59	2	1	62
30-39	78	1	1	80
40-49	58	3	1	62
50-59	32	2	0	34
60-69	20	1	1	22
>70	6	2	3	11
<b>TOTAL</b>	<b>280</b>	<b>12</b>	<b>8</b>	<b>300</b>

The TABLE- 7 shows the age distribution of various thyroid lesions according to the conventional cytological method. The highest number of cases occurred in the age group of 30-39 years and the cases were predominantly benign reported under this age group. The maximum number of cases in the category of follicular neoplasm presented in middle age. The

lesions classified as malignant most commonly presented in seventh decade of life.[CHART-22]

**AGE WISE DISTRIBUTION OF THYROID LESIONS ACCORDING TO CONVENTIONAL METHOD [CHART-22]**



***CHART 22 : Age wise distribution of thyroid lesions according to conventional method***

## **CYTOLOGICAL DIAGNOSIS BY BETHESDA CLASSIFICATION**

### **CATEGORY I (NON DIAGNOSTIC ) :**

Out of 300 patients, 3 cases (1%) the aspirates were unsatisfactory and were diagnosed under nondiagnostic or unsatisfactory category.

### **CATEGORY II (BENIGN) :**

This category included most of the cases in the study with 274 cases (91.3%) out of the total 300 cases. It consists of non- neoplastic or negative for malignancy cases like colloid goitre with 52 cases (17.3% ), adenomatoid nodule 131 cases (43.7% ), granulomatous (subacute ) thyroiditis 1 case (0.3%), hashimoto's thyroiditis 90 cases (30%).

### **CATEGORY III (AUS/FLUS) :**

This category includes lesions which were not either clearly benign or malignant. The conclusive opinion is difficult in this category. we had 1 case (0.3%) under this category.

### **CATEGORY IV(FN/ SFN) :**

Under this category we had 12 cases (4%) of the total 300 cases reported as follicular neoplasm.

### **CATEGORY V (SFM) :**

This category includes 2 cases (0.7%) out of the total 300 cases in our study.

### **CATEGORY VI (Malignant) :**

This category includes 8 cases (2.7% ) out of the total 300 cases in our study and all of them comprising of papillary carcinoma thyroid.

### **PERCENTAGE OF DIFFERENT CATEGORIES OF THYROID LESIONS ACCORDING TO BETHESDA [TABLE-7]**

#### **BETHESDA CATEGORY**

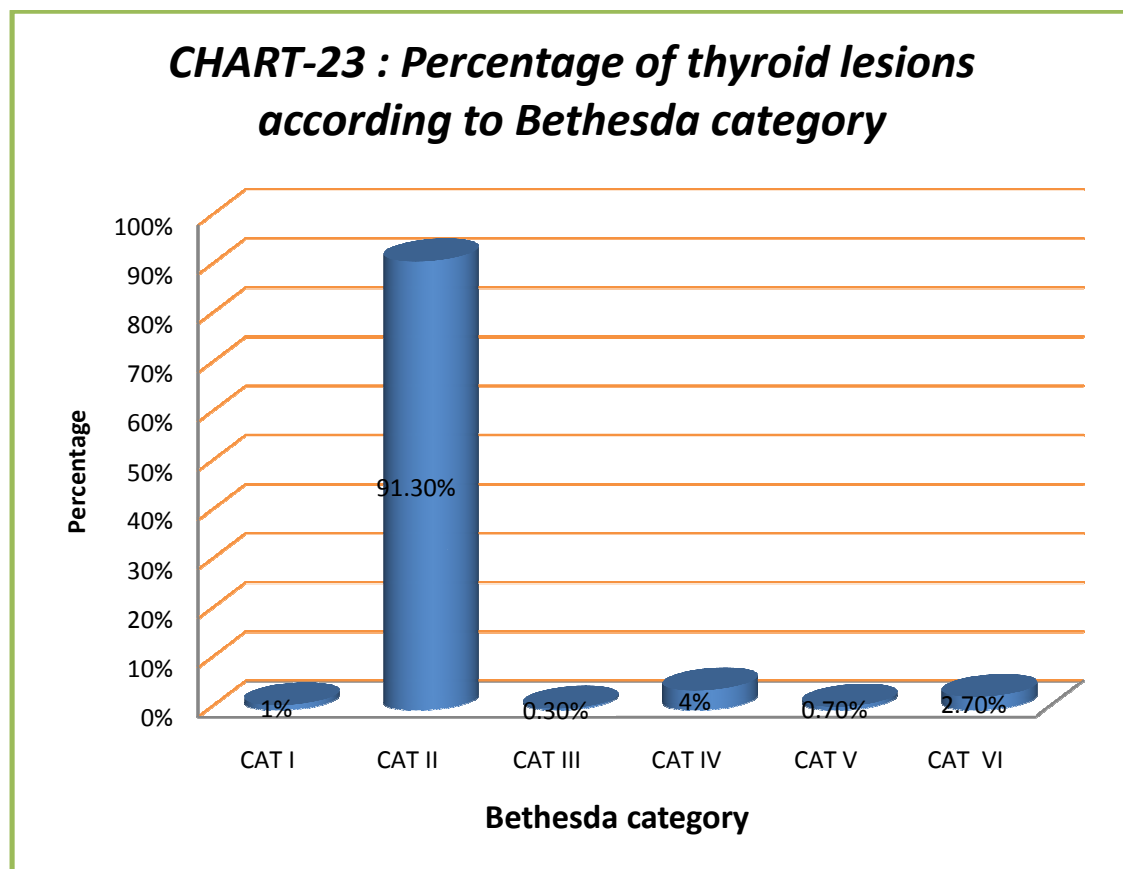
***TABLE- 8 : Classification of thyroid lesions in Bethesda system.***

<b>BETHESDA CATEGORY</b>	<b>NO: OF CASES</b>	<b>PERCENTAGE</b>
CAT I : NON DIAGNOSTIC	3	1
CAT II: BENIGN	274	91.3
CAT III: AUS / FLUS	1	0.3
CAT IV: FN/SFN	12	4
CAT V : SFM	2	0.7
CAT VI : MALIGNANT	8	2.7
TOTAL	300	100

Out of the total 300 thyroid cases presented in our study, by classifying lesions in conventional cytological classification 292 cases were diagnosed under benign category and the remaining 8 cases were diagnosed as malignant, by classifying the lesions in Bethesda out of the total 292 cases

diagnosed under benign category by conventional cytology, 3 cases were classified in Non – diagnostic category, 1 case was classified in the category of Atypia of undetermined significance / follicular lesion of undetermined significance, 2 cases were classified in the category of Suspicious for malignancy, 12 cases were classified under the category of Follicular neoplasm/ Suspicious for follicular neoplasm, and the rest of the cases were classified in the category of Benign follicular nodule. In malignant category 8 cases were seen.[TABLE-8,CHART-23]

**PERCENTAGE OF THYROID LESIONS BY CLASSIFYING IN BETHESDA SYSTEM [CHART-23]**



## AGE GROUP ACCORDING TO BETHESDA CLASSIFICATION

[TABLE-9],[CHART-24]

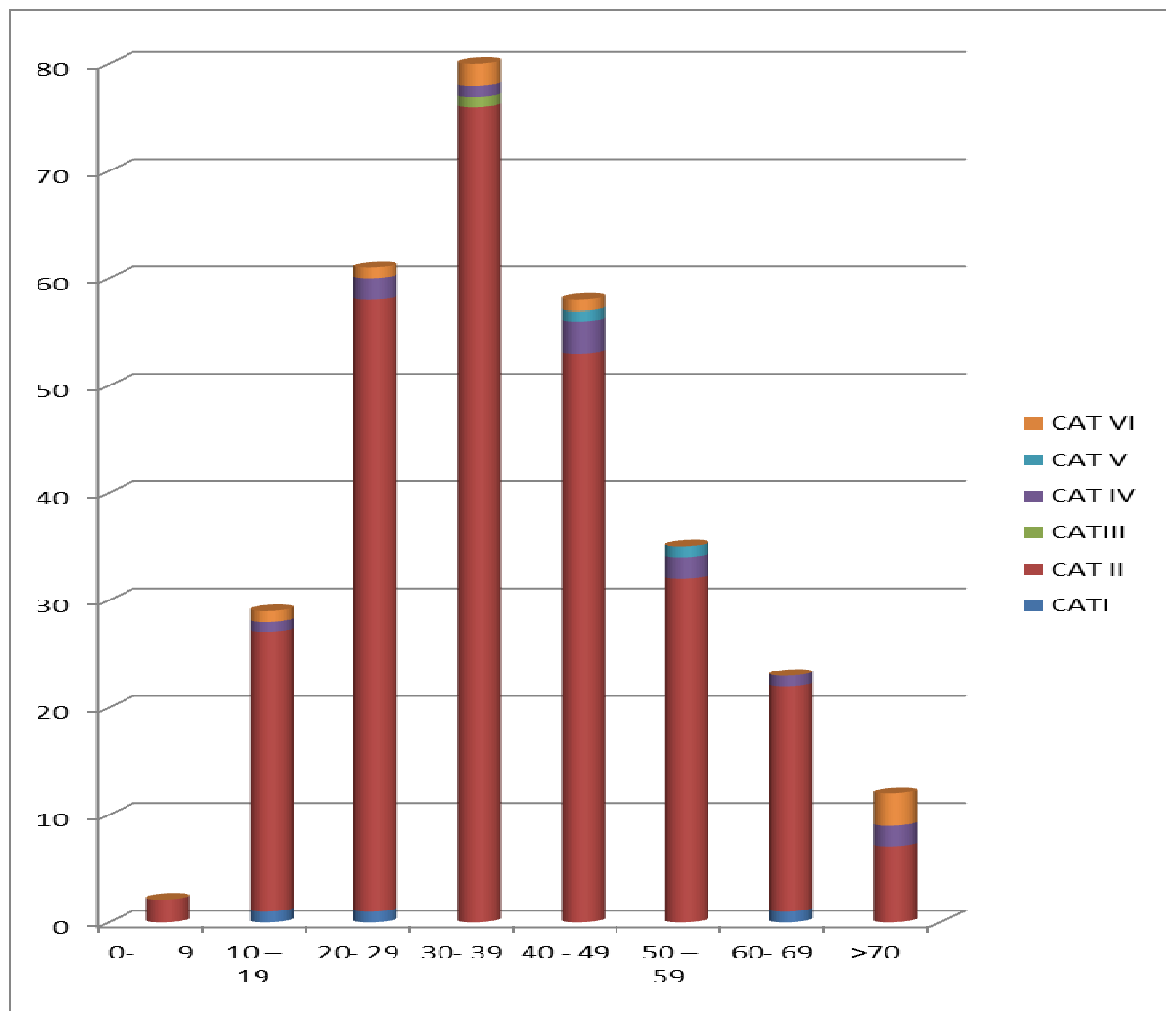
*Table 9 : No : of cases in Bethesda category according to age group*

AGE IN YRS	CAT I	CAT II	CAT III	CAT IV	CAT V	CAT VI
0- 9	0	2	0	0	0	0
10 – 19	1	26	0	1	0	1
20- 29	1	57	0	2	0	1
30- 39	0	76	1	1	0	2
40 - 49	0	53	0	3	1	1
50 – 59	0	32	0	2	1	0
60- 69	1	21	0	1	0	0
>70	0	7	0	2	0	3
TOTAL	3	274	1	12	2	8

The above table shows the number of cases in different age group according to Bethesda. In all age groups the maximum number of cases were present in Category II. In 0-9 yr age group 2 cases were present and both were diagnosed under Category II. Category I showed 3 cases in the age group ranging from 10-69 years. There was 1 case diagnosed in Category III in the age group of 30-39 years. In Category IV cases were present in all age

groups except in 0-9 yrs age group. Category V had 2 cases in the age group of 40-59 years. In Category VI there were cases in all age group except 0-9yrs and 40-59 years and maximum number of cases were seen after the seventh decade of life in this category. [TABLE -8],[CHART -24].

### **NO OF CASES ACCORDING TO BETHESDA CATEGORY IN AGE GROUP [CHART-24]**



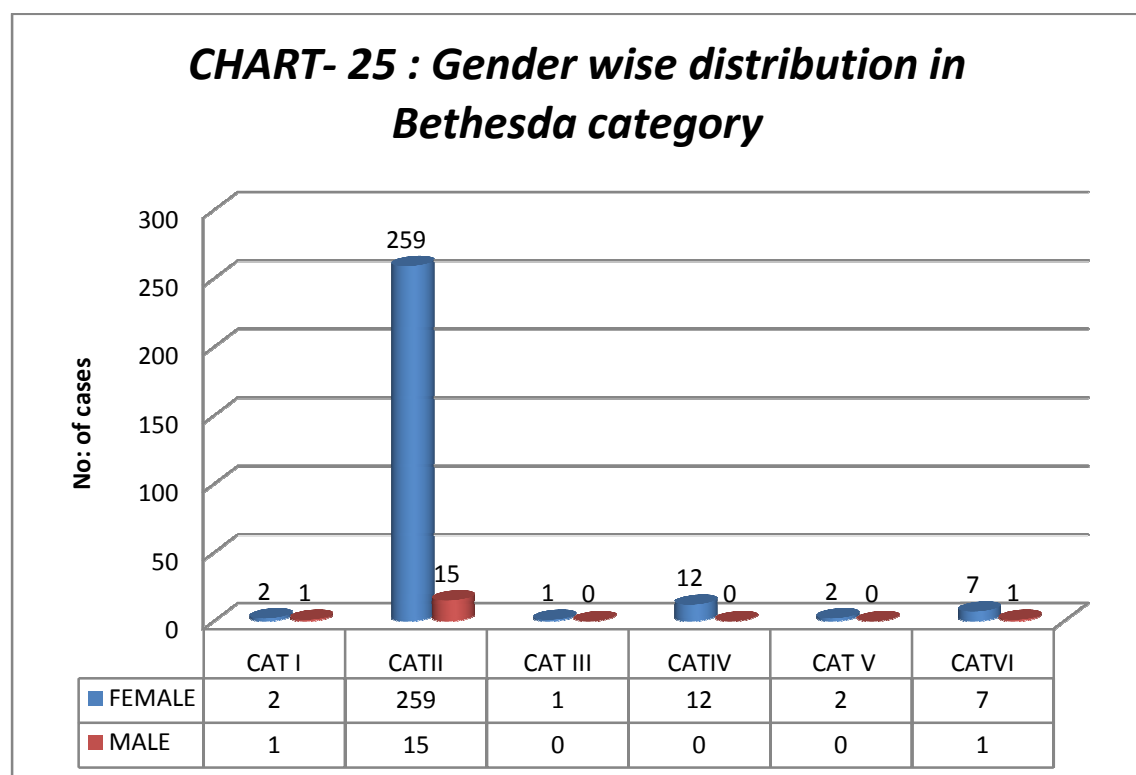
***CHART- 24 : No : of cases according to age group in Bethesda category***



**GENDER WISE DISTRIBUTION ACCORDING TO BETHESEDA  
CLASSIFICATION [TABLE-10],[CHART -25]**

**TABLE- 10 : Gender wise distribution according to Bethesda category**

<b>GENDER</b>	<b>CAT I</b>	<b>CAT II</b>	<b>CAT III</b>	<b>CAT IV</b>	<b>CAT V</b>	<b>CAT VI</b>
MALE	1	15	0	0	0	1
FEMALE	2	259	1	12	2	7



The TABLE-10 and CHART-25 shows the number of cases distributed according to gender in each category of the Bethesda system. The maximum number of cases were present in Category II in both male and

female population. In Category I average number of cases were present in both genders. In Category III, IV and V, cases were present in female population while the male population had no cases. In Category VI the highest number of cases were present in female population compared to males.

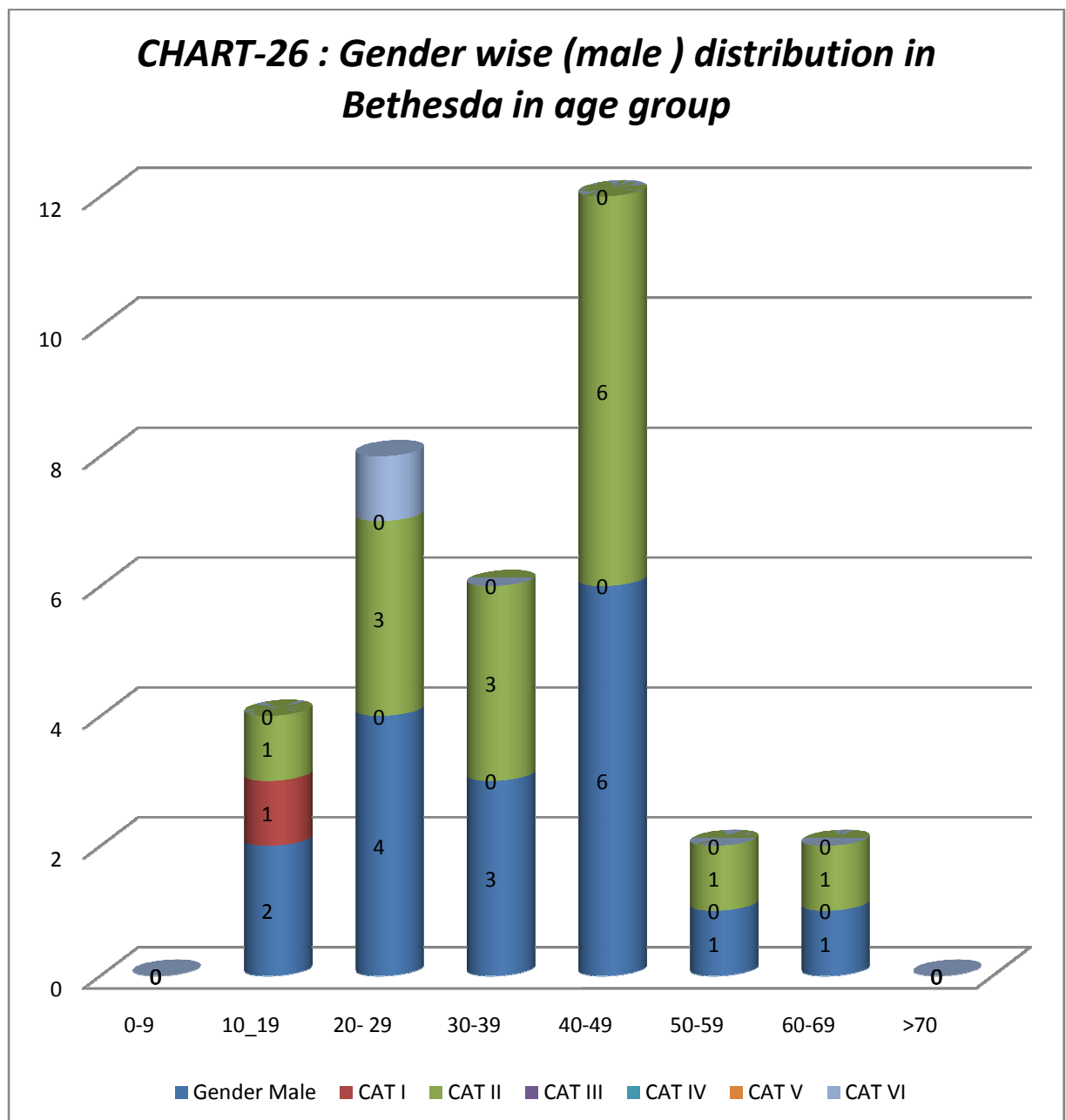
**GENDER WISE (MALE) DISTRIBUTION ACCORDING TO AGE GROUP BY BETHSEDA [TABLE-11], [CHART-26]**

***TABLE -11 : Gender wise (male) distribution in Bethesda in age group***

<b>Age in Years</b>	<b>Gender Male</b>	<b>CAT I</b>	<b>CAT II</b>	<b>CAT III</b>	<b>CAT IV</b>	<b>CAT V</b>	<b>CAT VI</b>
0-9	0	0	0	0	0	0	0
10-19	2	1	1	0	0	0	0
20- 29	4	0	3	0	0	0	1
30-39	3	0	3	0	0	0	0
40-49	6	0	6	0	0	0	0
50-59	1	0	1	0	0	0	0
60-69	1	0	1	0	0	0	0
>70	0	0	0	0	0	0	0

The TABLE-11 and the CHART-26 shows the number of cases according to age group in male population in the present study according to Bethesda classification. There were no case in the 0-9 yr age group in all

Categories. In 10-19 yr age group cases were present in Category I and Category II. The 20-29 yr age group had cases in Category II and Category VI. In 30-39,40-49,50-59,60-69 age groups cases were present only in Category II. In the age group > 70 years had no cases in any of the Categories.



**GENDER WISE DISTRIBUTION (FEMALE ) IN AGE GROUP BY BETHESDA [TABLE-12], [CHART -27]**

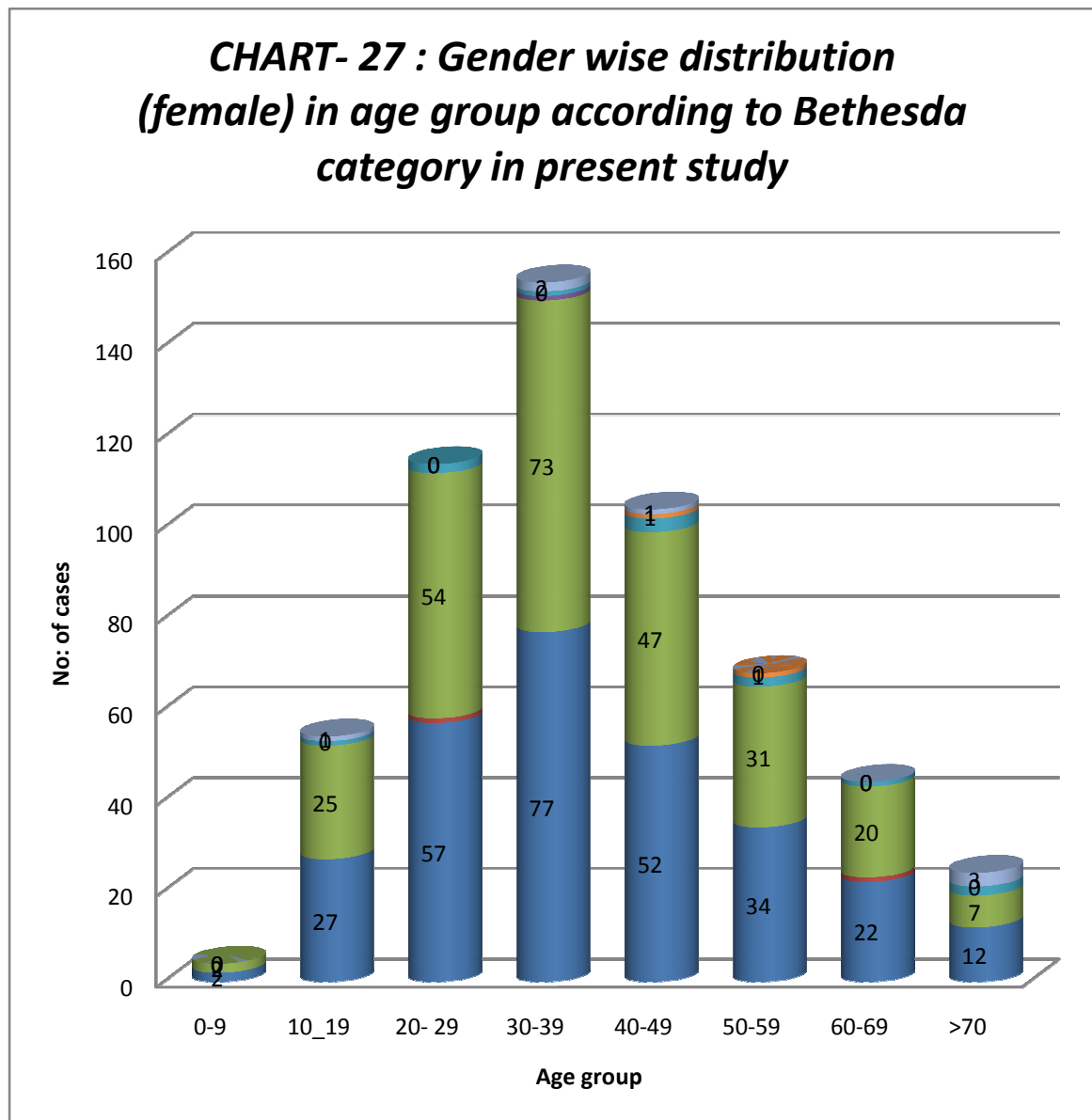
***TABLE- 12 : Gender wise distribution (female) in Bethesda according to age group***

<b>AGE IN YEARS</b>	<b>GENDER FEMALE</b>	<b>CAT I ND</b>	<b>CAT II BENIGN</b>	<b>CAT III AUS</b>	<b>CAT IV FN/SFN</b>	<b>CATV SFM</b>	<b>CAT Malignant</b>
0-9	2	0	2	0	0	0	0
10-19	27	0	25	0	1	0	1
20- 29	57	1	54	0	2	0	0
30-39	77	0	73	1	1	0	2
40-49	52	0	47	0	3	1	1
50-59	34	0	31	0	2	1	0
60-69	22	1	20	0	1	0	0
>70	12	0	7	0	2	0	3

The TABLE-12 and the CHART-27 shows the number of cases in each age group according to Bethesda classification in the present study in the female population. The Category II had the highest number of cases compared to all other categories in all age groups. In 0-9 yrs age group cases were present only in Category II. In 10-19 yrs age group cases were present in Category II, IV and VI. In 20-29 yrs age group cases were present in Category I, II and IV. In 30-39 year age group cases were present in Category II, III, IV. In the

age group of 40-49 years cases were present in Category II, IV,V, VI. In 50-59 year age group cases were present in Category II, IV, and V. In 60-69 years age group cases were present in Category I, II,and IV. In the age group of above 70 years cases were present in Category II, IV and VI.

**GENDER WISE DISTRIBUTION OF (FEMALE ) IN AGE GROUP ACCORDING TO BETHESEDA**



## **CYTOLOGICAL FEATURES OF BENIGN NODULES**

Among the 274 cases (91.3%) reported as benign under Bethesda category, 52 cases (17.3%) had cytological features consistent with colloid nodule and 131 cases (43.7%) had cytological feature consistent with adenomatoid nodule, 90 cases (30%) had cytological features consistent with Hashimoto's thyroiditis.

Of the 52 cases reported as colloid goitre all the 50 cases (96.1%) had benign thyroid follicular cells arranged predominantly in clusters and sheets in 2 cases. The background colloid quality was thin in majority of cases. The amount of colloid in background was of moderate amount in majority of the cases and abundant amount in some cases. Some cases showed lymphocytes, macrophages also in the background of the smear diagnosed as colloid nodule. The thyroid follicular epithelial cells were of normal size in all clusters with no pleomorphism.

Of the 90 cases (30%) that are reported as "consistent with lymphocytic (Hashimoto) thyroiditis in a proper clinical context", all of them had Hurthle cells changes in the follicular cells and the Hurthle cells were predominantly seen in clusters and in few smears the Hurthle cells were seen arranged in sheets. Lymphocytic background was seen predominantly in all cases of Hashimoto's thyroiditis and few cases showed macrophages.

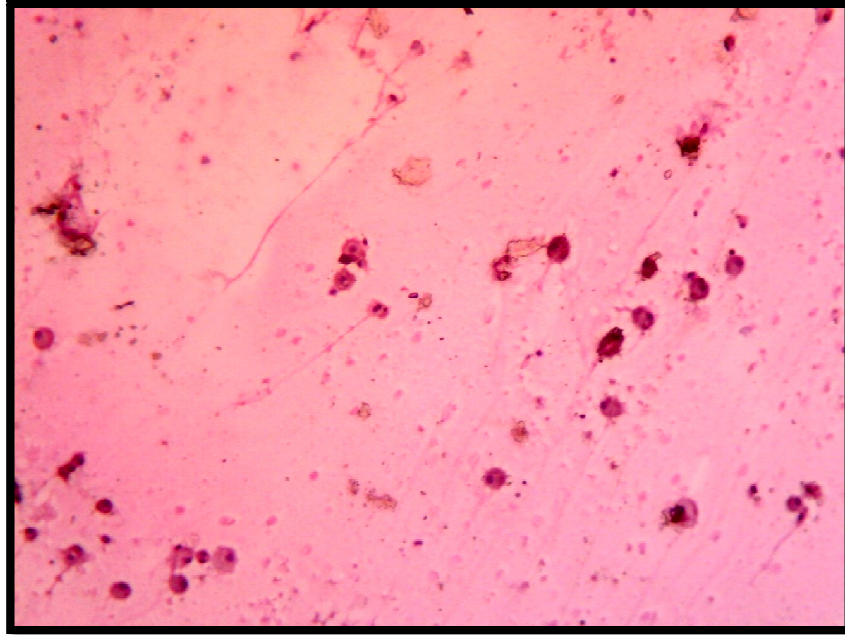
## **CYTOLOGICAL FEATURES OF PAPILLARY CARCINOMA**

Out of the total 300 cases, 12 cases that were reported as papillary carcinoma according to Bethesda, and all the 12 cases had marked cellularity and papillary fragments seen in 100 % of cases with individual cells showing oval shaped cells (75%), and pleomorphism in few cells. The individual cells showed moderate amount of eosinophilic cytoplasm(100%).

The nucleus was oval (75%) to round (25%) in shape, ground glass appearance (100%) with powdery chromatin (100%), nuclear grooves (100%), nuclear inclusions (100%) and prominent nucleoli. Hurthle cell changes were noted in (100 % ) of cases. Background showed lymphocytes and haemorrhage in (100% ) of cases. Psammoma bodies were not seen in any of these cases.

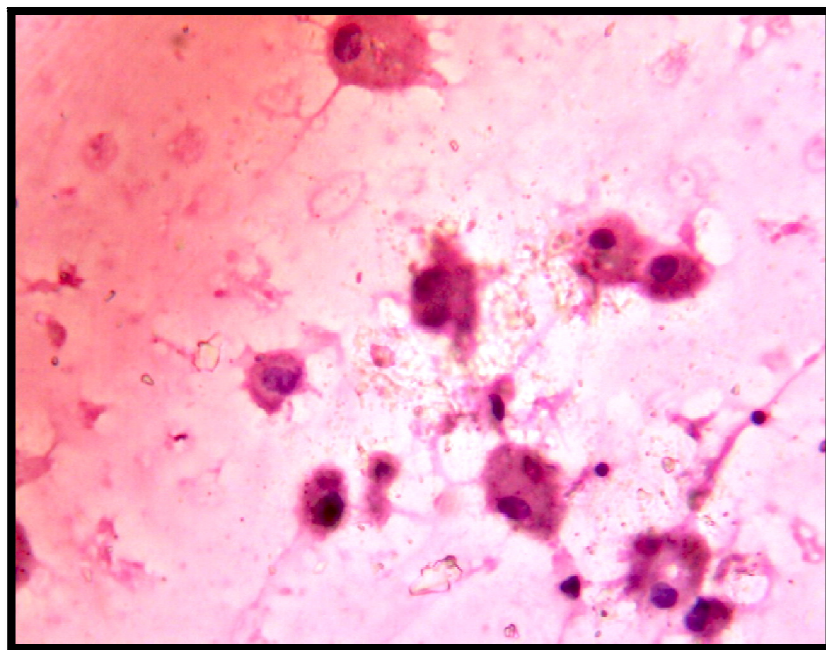
## **CYTOLOGICAL FEATURES OF FOLLICULAR NEOPLASM**

Of the 12 cases (4%) cytologically reported as follicular neoplasm according to Bethesda classification, 9 cases (75% ) had marked cellularity and 3 cases (25%) had moderate cellularity. The cytological features include microfollicles in (100%) of cases and cell clusters in (100%) of cases. Individual cells were uniform in 100% of cases, round (76.9%) to oval (23.1% ) with moderate amount of cytoplasm in (100%) of cases and the cytoplasm is eosinophilic in (91.7%) of cases and basophilic cytoplasm in (8.3%) of cases. The nucleus were round in shape in (83.3%) of cases and oval in shape in (16.7%) of cases and exhibiting nuclear hyperchromatism in (66.7%) of cases. Background showed haemorrhage in (83.3% ) of cases and colloid in moderate amount (16.7%) of cases.



*Figure -1*

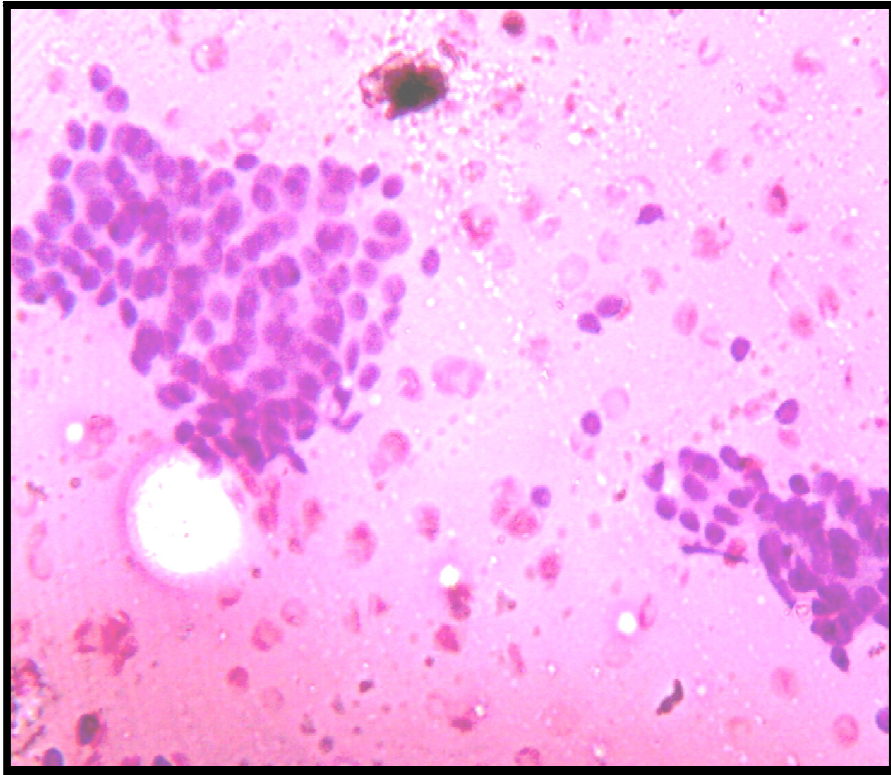
*Nondiagnostic. Cystic macrophages are seen in sheets H&E , 100x*



*Figure -2*

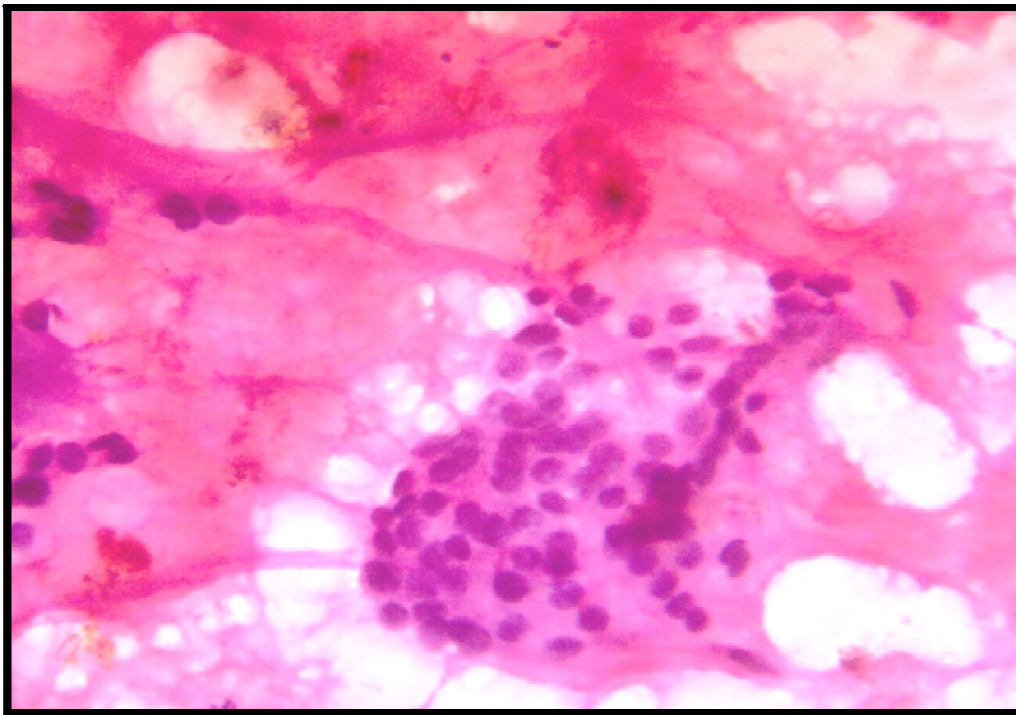
*Nondiagnostic .Cystic macrophages with abundant cytoplasm and contains hemosiderin pigment, H&E , 400x*



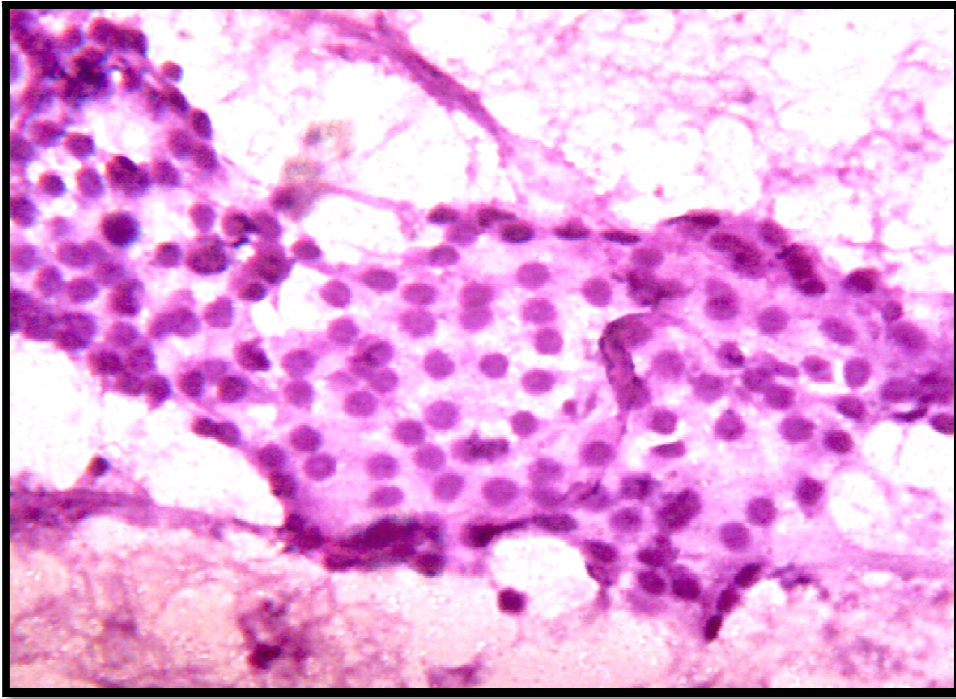


**Figure -3**

***Benign follicular nodule. Nuclear overlapping in the form of folded Sheets is observed . Watery colloid is present in the background , H&E,. 400x***

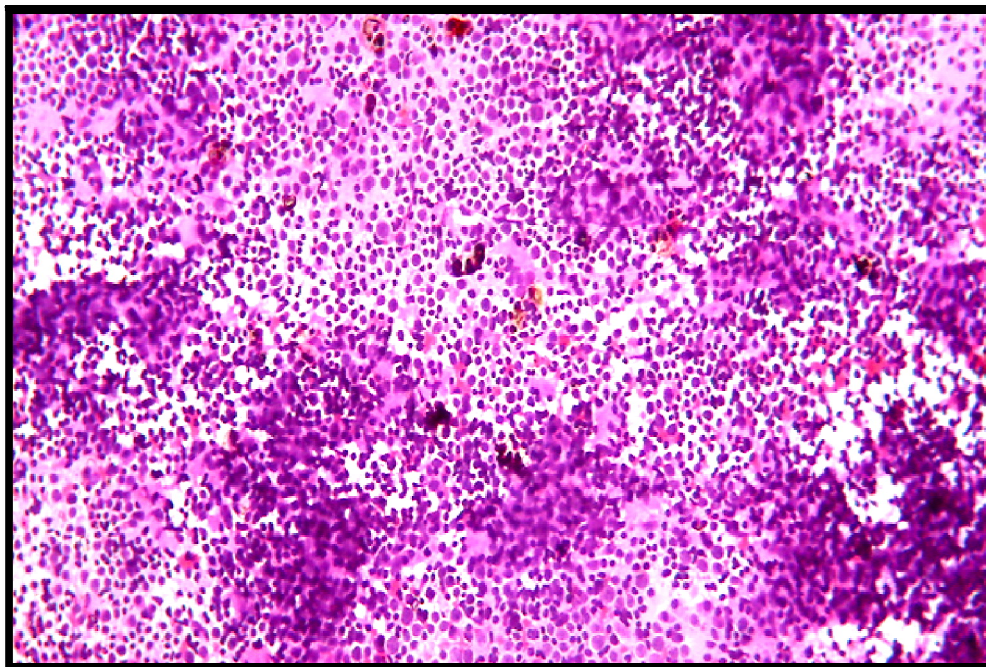


***Figure -4 Benign follicular nodule (Nodular goitre). Benign follicular cells arranged in clusters and have round to oval nuclei with finely granular chromatin and inconspicuous nucleoli, H& E , 400x***



**Figure-5**

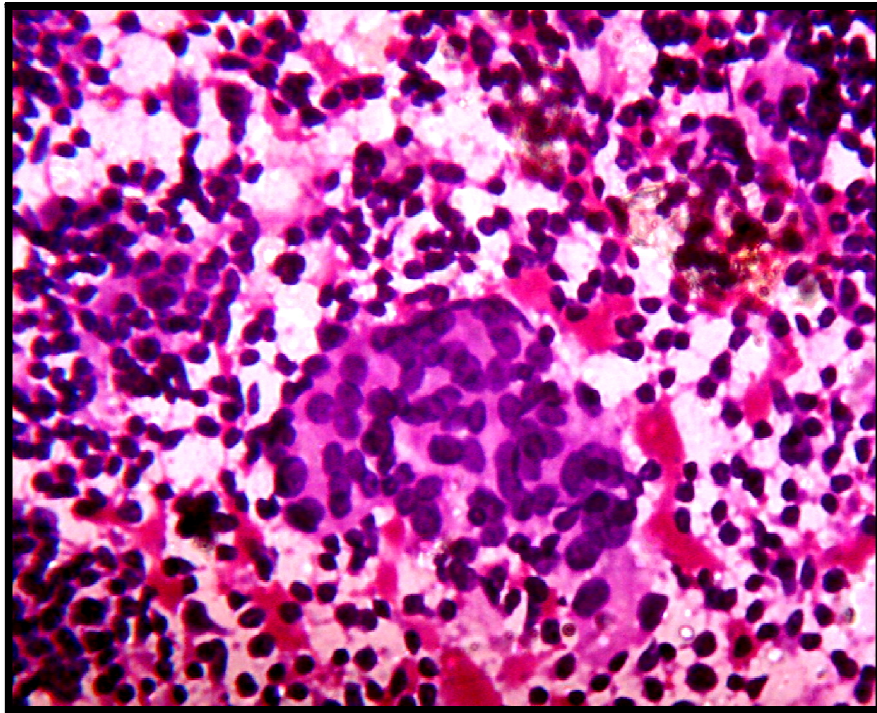
*Benign follicular nodule(Adenomatoid nodule). Monolayered sheets of follicular cells , moderate amount of pale cytoplasm , monomorphic nuclei , inconspicuous nucleoli, H&E stain , 400x*



**Figure -6**

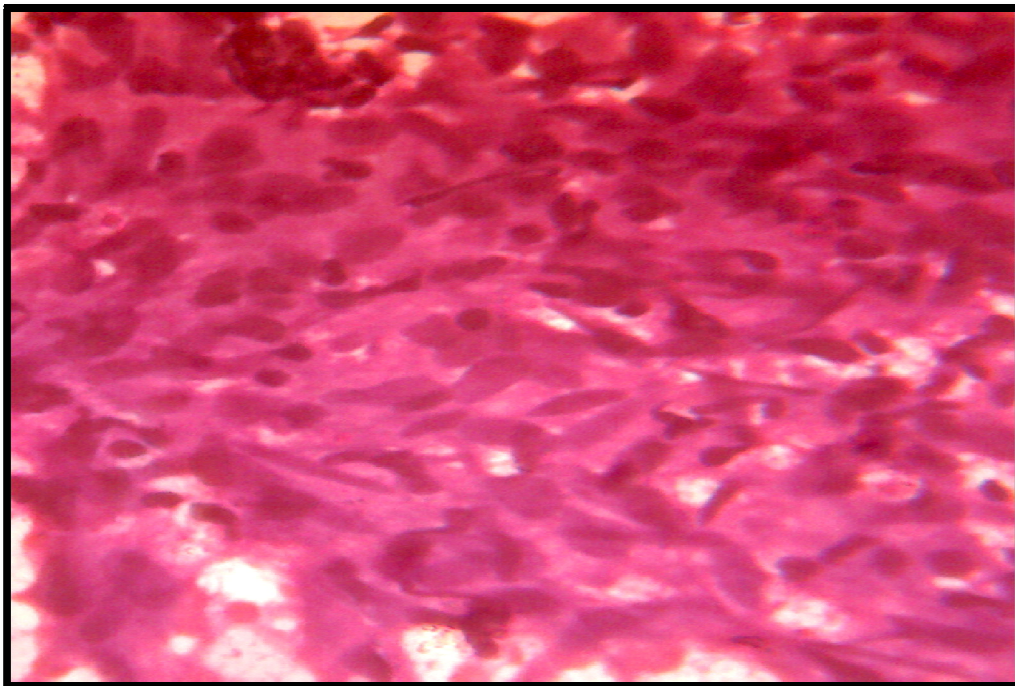
*Lymphocytic (Hashimoto's) thyroiditis. There is a mixed population of Hürthle cells and polymorphic lymphocytes , H&E stain , 100x view*





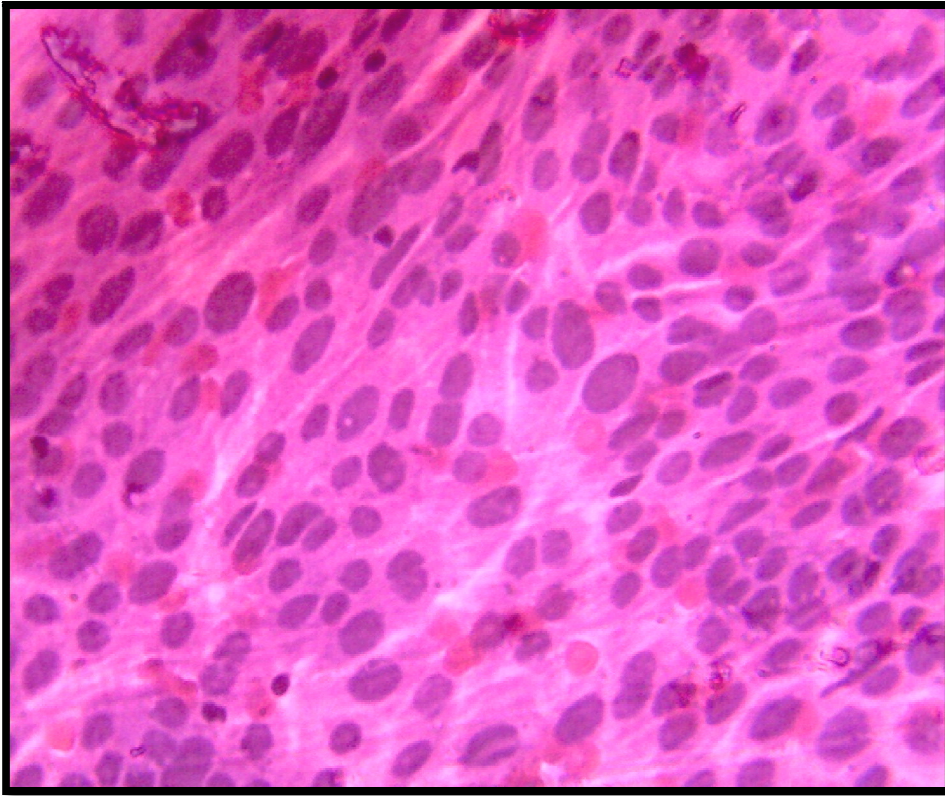
*Figure -7*

*Lymphocytic (Hashimoto's) thyroiditis. There is a mixed population of Hürthle cells and polymorphic lymphocytes , H&E , 400x view*



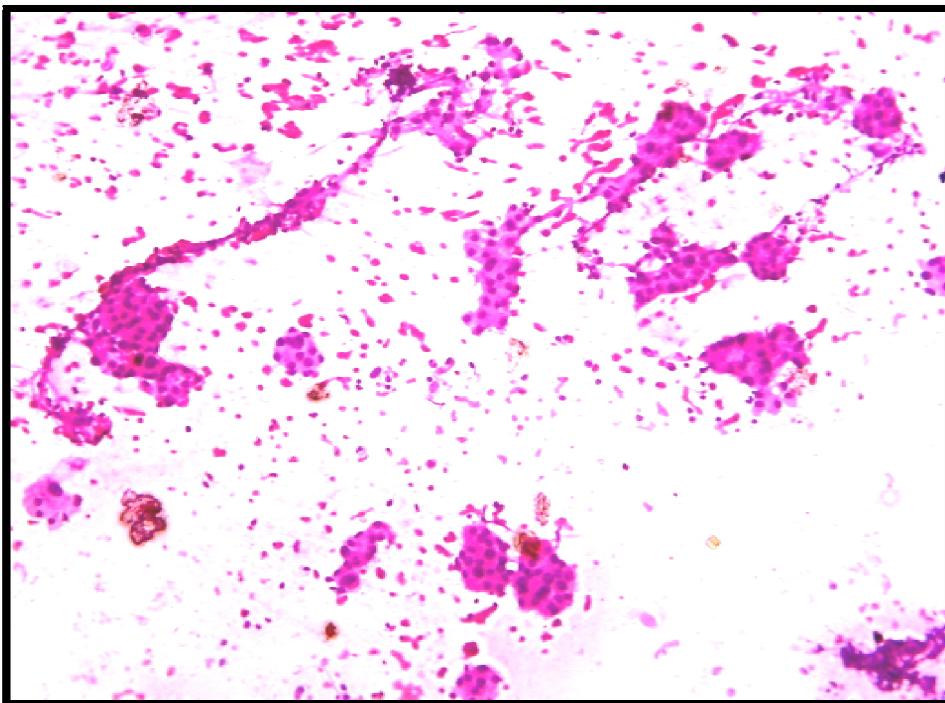
*Figure -8*

*Granulomatous (subacute) thyroiditis. Epithelioid cells in sheets mixed inflammatory cells, and benign follicular cells are present , H&E , 400x*



**Figure - 9**

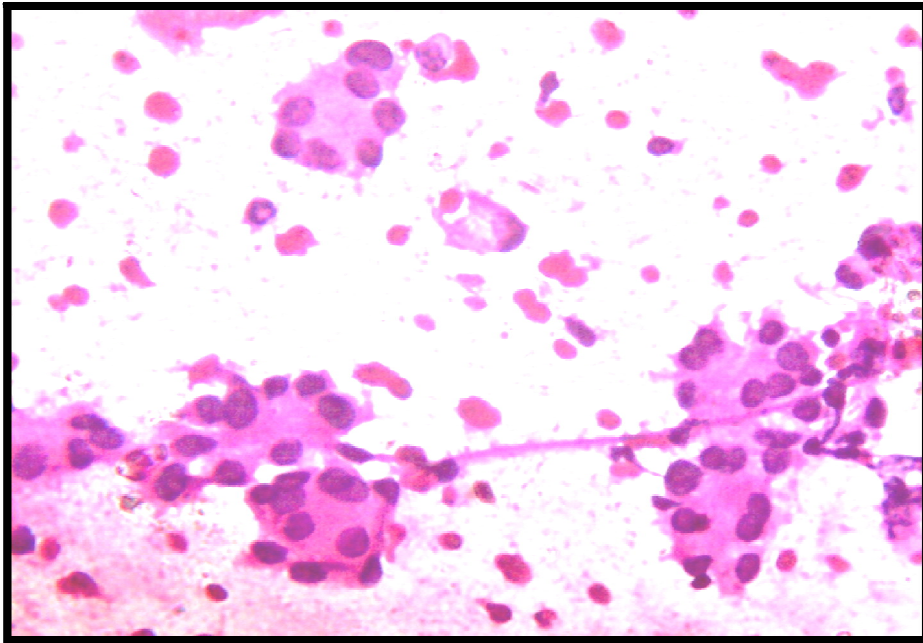
***AUS : Sheets of thyroid follicular cells , in diffuse sheets and some in microfollicle pattern , with mild nuclear and cytoplasmic enlargement , some of the nuclei showing nuclear inclusion ,H&E stain ,400x***



**Figure -10**

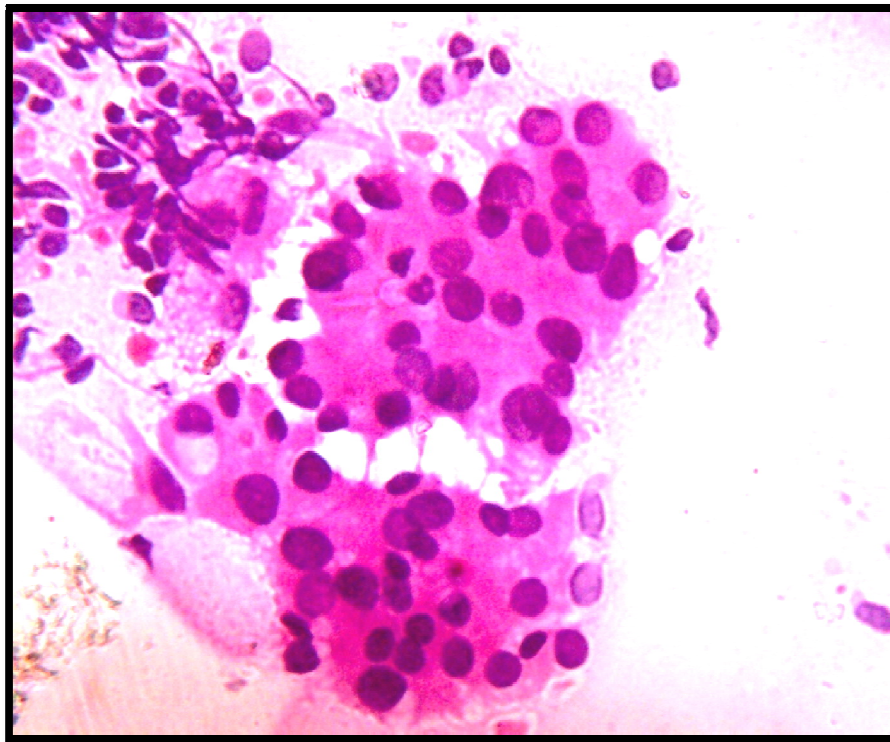
***Follicular neoplasm/Suspicious for a follicular neoplasm. Folliculacells are arranged as microfollicles having monomorphic nuclei and moderate cytoplasm , H& E ,100x***





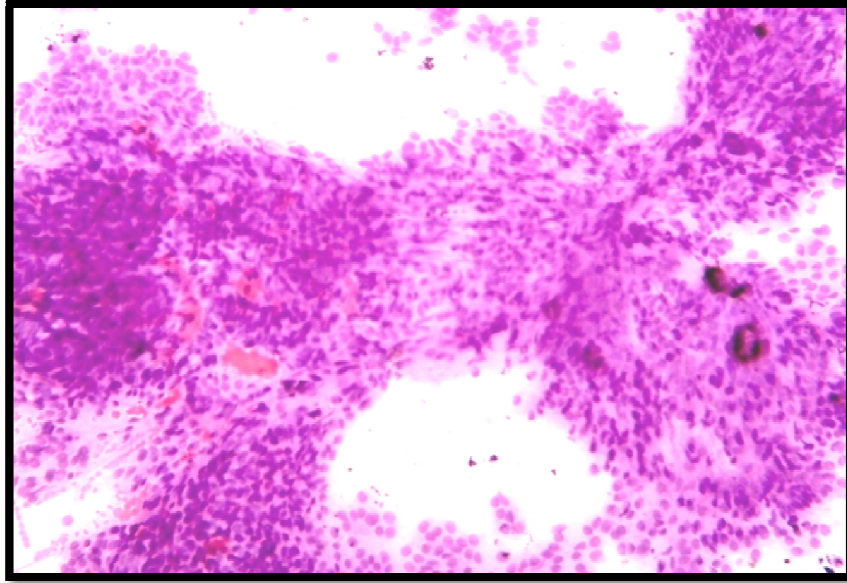
***Figure -11***

***Follicular neoplasm/Suspicious for a follicular neoplasm. Follicular cells are arranged as microfollicles and have round nuclei, H&E stain , 400x***



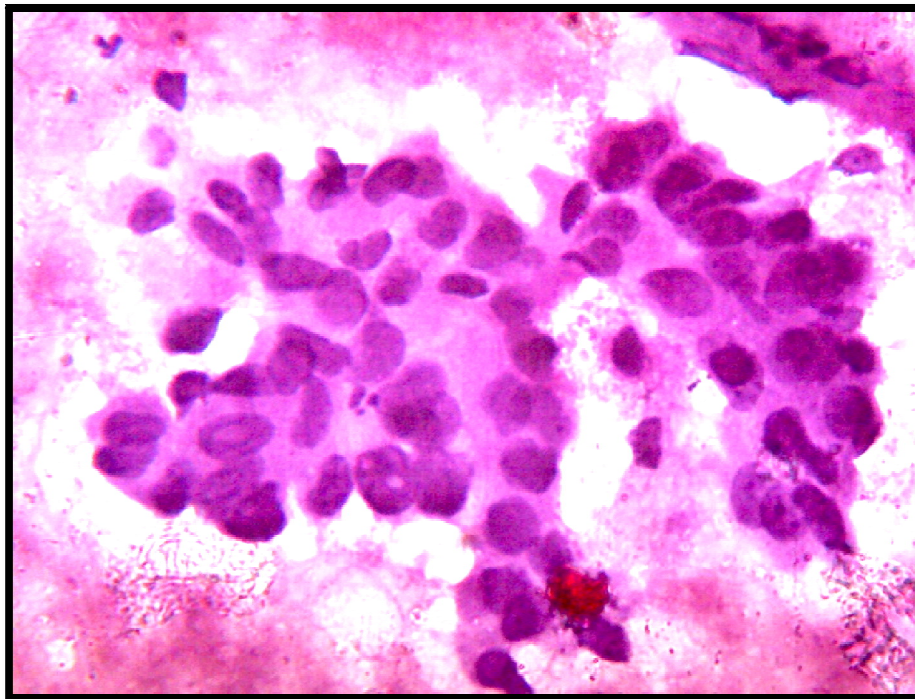
***Figure -12***

***Follicular neoplasm/Suspicious for a follicular neoplasm. Follicular cells in crowded, microfollicular arrangements show slight size variation in nuclear size ,inconspicuous nucleoli . H&E stain , 400x***



**Figure -13**

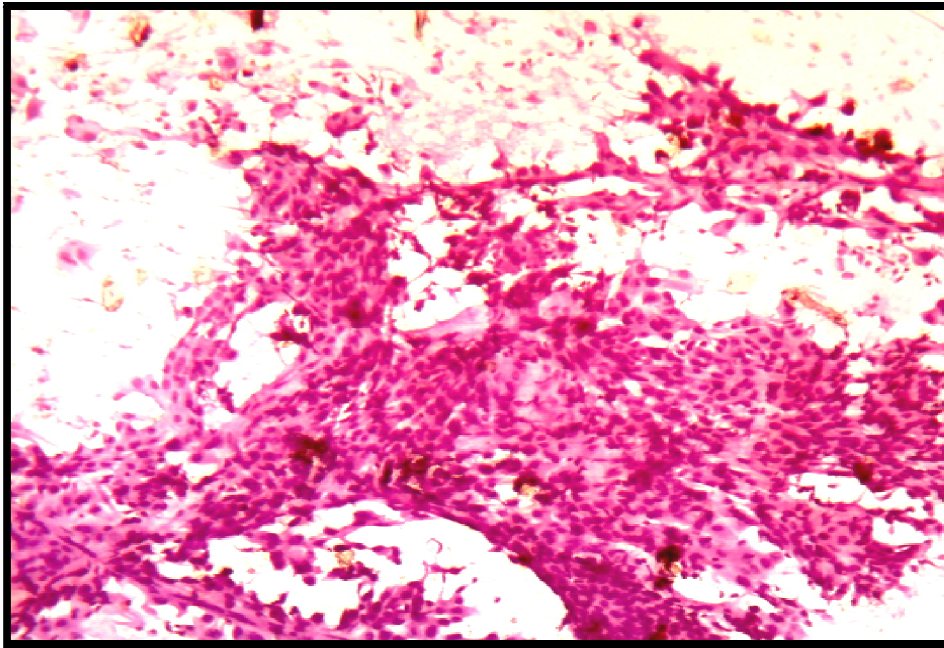
*Suspicious for papillary thyroid carcinoma. The follicular cells arranged in papillary pattern, nuclear enlargement ,nuclear crowding,H&E ,100x*



**Figure -14**

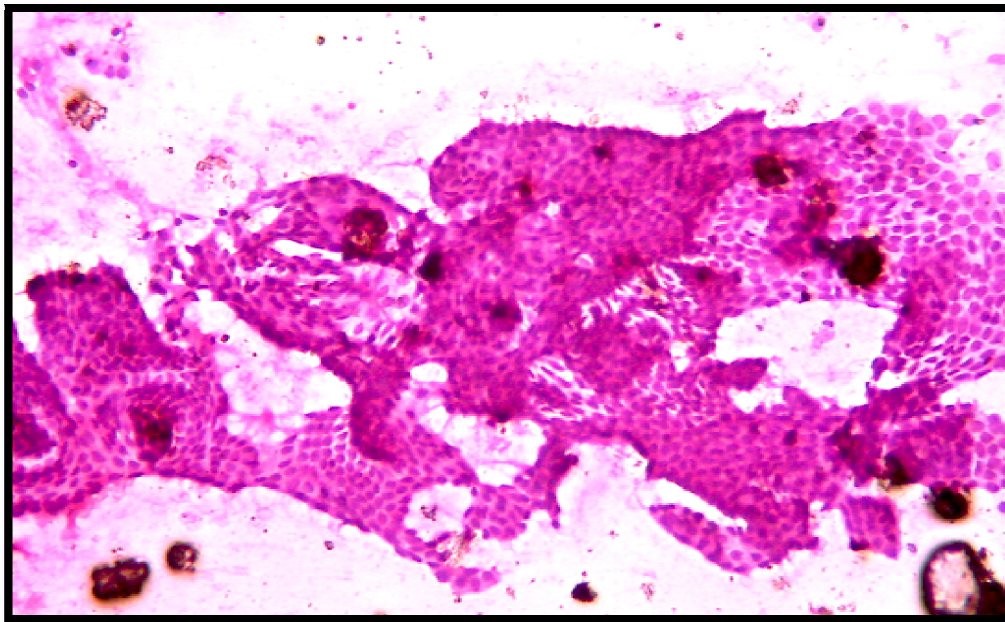
*Suspicious for papillary thyroid carcinoma: Follicular cells are arranged in papillae,with few nucleus showing nuclear grooves and nuclear pseudoinclusion, H&E, 100x*





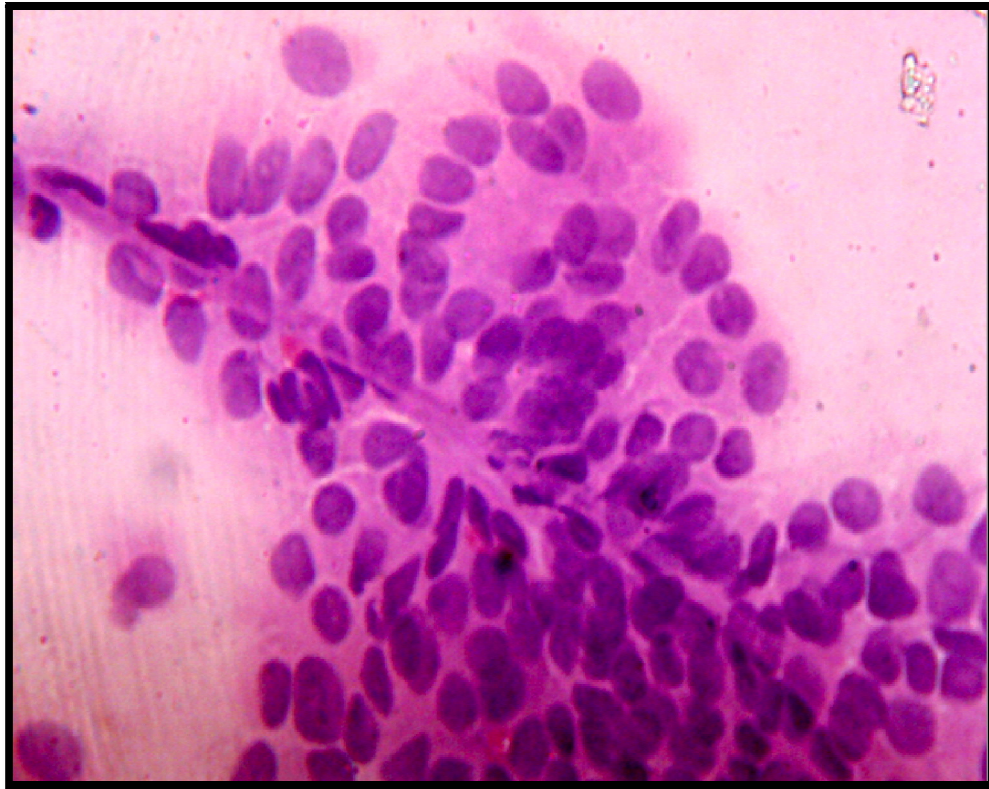
*Figure -15*

*Papillary thyroid carcinoma: Follicular cells are arranged in papillae, marked crowding of the neoplastic cells that line the papillae,H&E,100x*

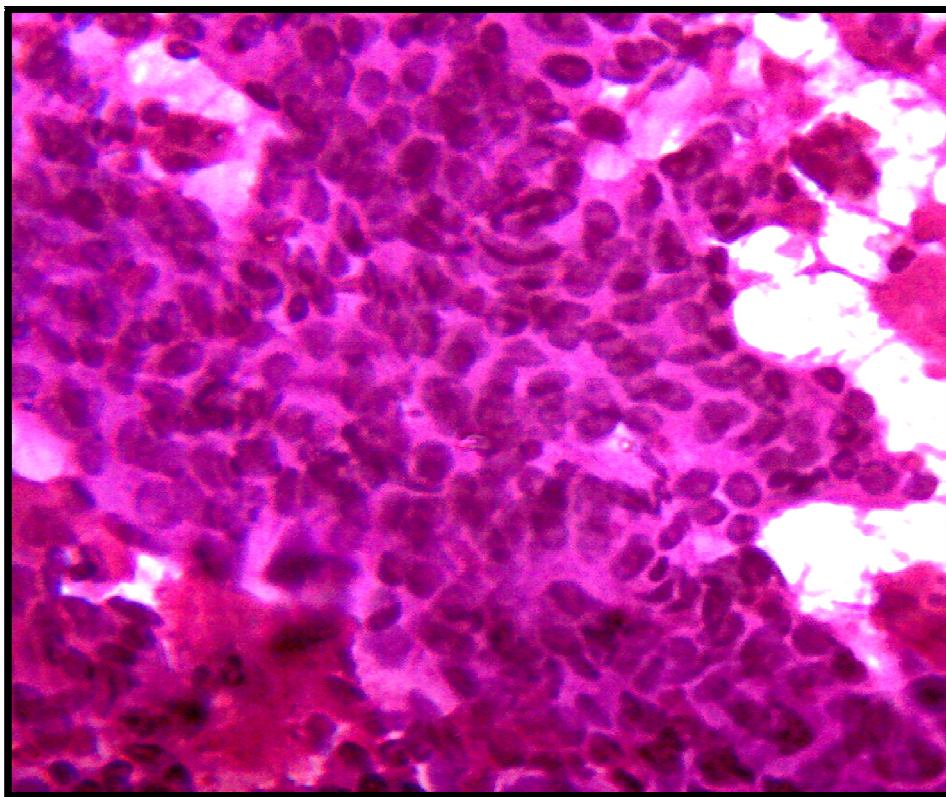


*Figure -16*

*Papillary thyroid carcinoma : Thyroid follicular epithelial cells arranged in monolayered sheets forming anatomical border,H&E , 100x*

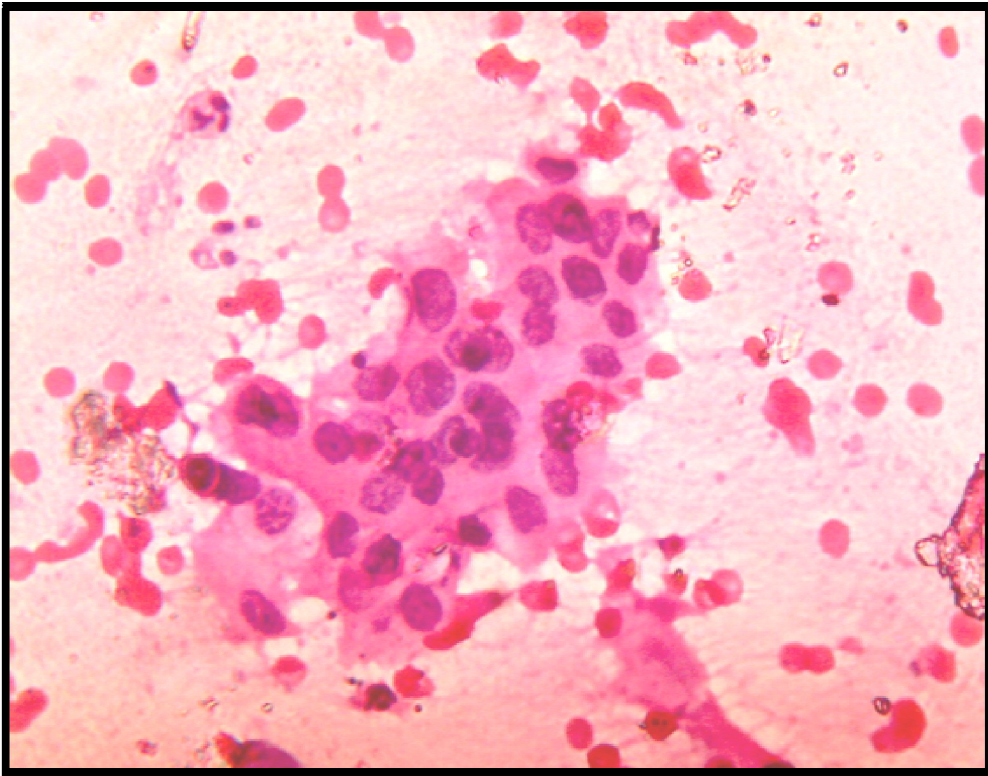


*Figure- 17*  
*Papillary thyroid carcinoma: Papilla with fibrovascular core,H&E,400x*

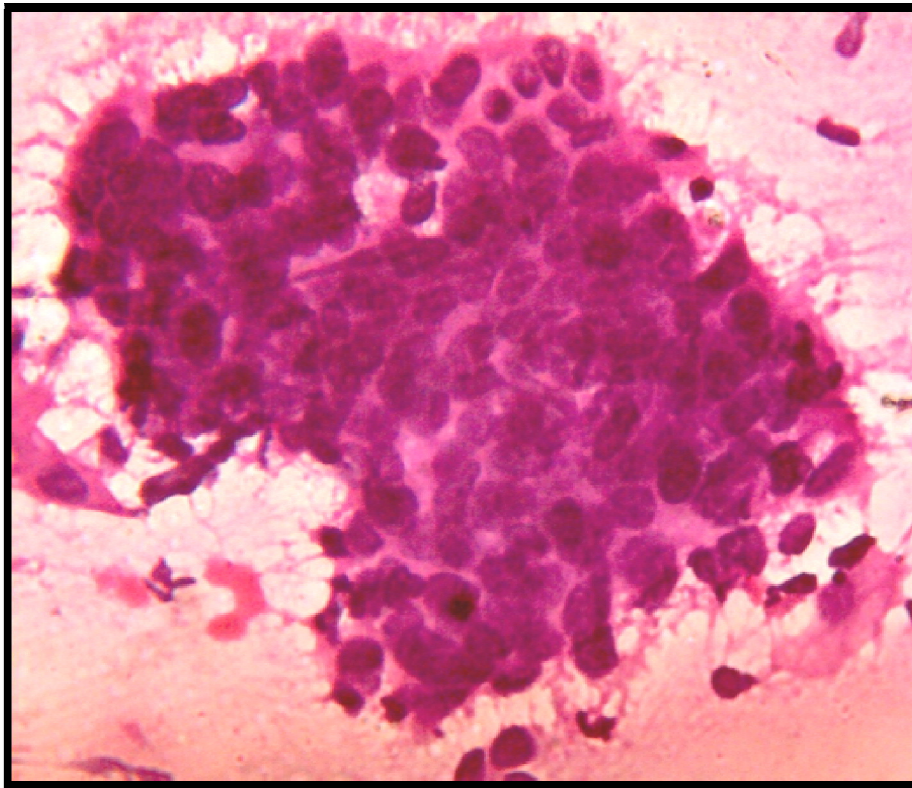


*Figure -18Papillary thyroid carcinoma: Follicular cells showing nuclear crowding, nuclear grooving,nuclear molding,H&E, 400x*

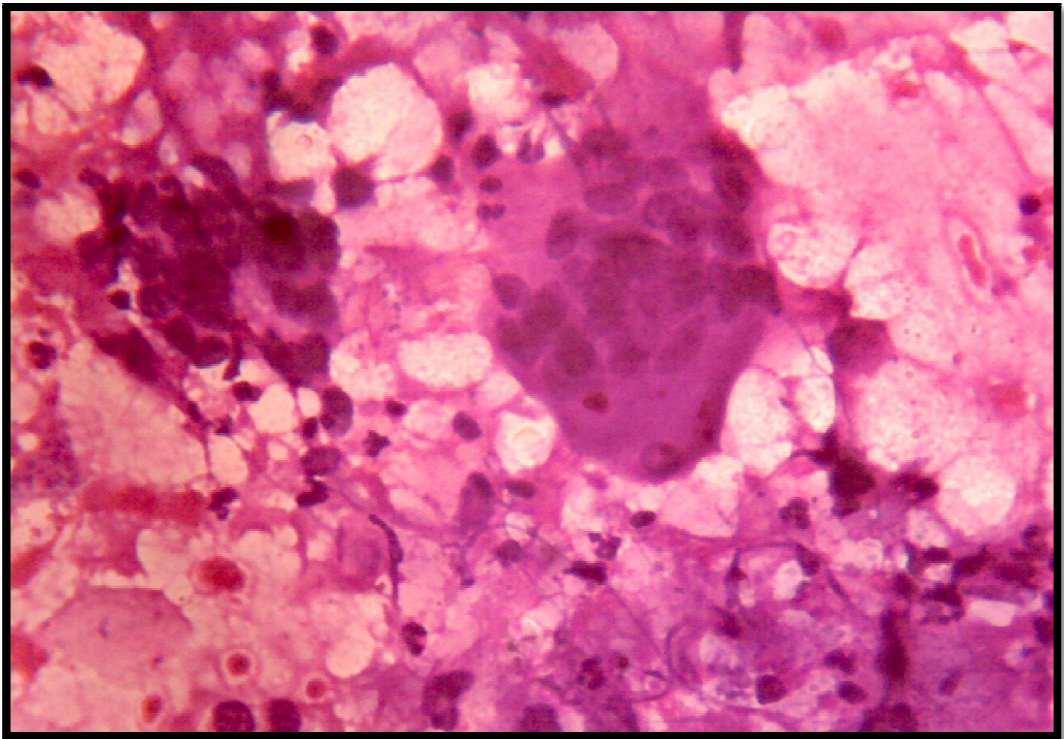




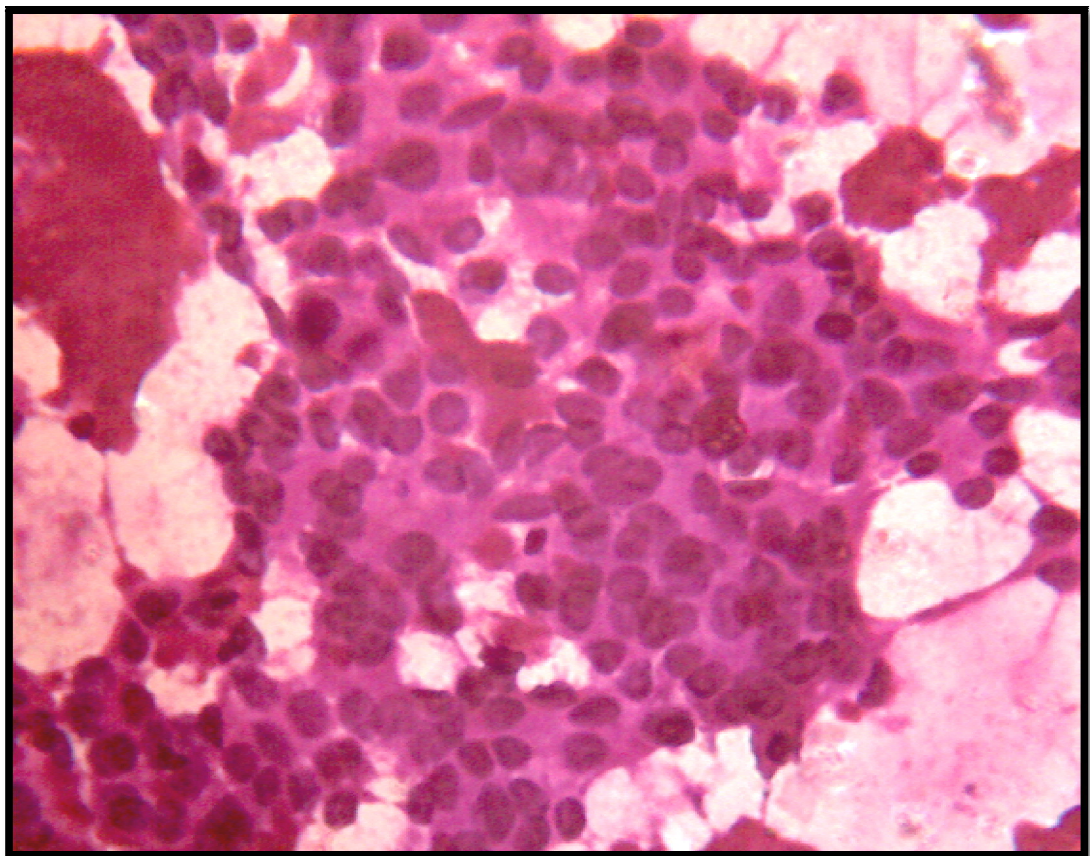
**Figure- 19**  
*Papillary thyroid carcinoma. Thyroid follicular cells in clusters , finely textured (powdery) chromatin, H&E,400x*



**Figure -20**  
*Papillary thyroid carcinoma: There is marked crowding of the neoplastic cells , nucleus showing powdery chromatin,H&E, 400x*



*Figure -21*  
*Papillary thyroid carcinoma showing Multinucleated giant cell ,H&E,400x*



*Figure- 22*  
*Papillary thyroid carcinoma:Follicular cells arranged in sheets ,few nuclei showing nuclear pseudoinclusion and nuclear grooving,H&E,400x*

## DISCUSSION

FNAC is the gold standard and the primary investigation of choice in the management of thyroid lesions along with the other investigations like ultrasonography (USG) examination, the thyroid function tests, thyroid scan, and the thyroid antibody levels are subsequently done to find out patients who require surgery and those who can be managed conservatively.<sup>[88]</sup> The reporting of the thyroid FNA suffers from the usage of “personalized”, local, institutional and descriptive terminologies. The ultimate goal of performing FNAC in the patients presenting with thyroid nodules is to diagnose the lesion as benign or malignant. The patients presenting with cytologic diagnosis suggestive of malignancy and/or neoplasia are treated surgically, while the patients presenting with the cytologic diagnoses of benign lesion can be followed up clinically.

The diagnosis of thyroid FNA differs from one institution to another institution. This difference is due to several factors, which include,

- a) The method by which the lesional tissue of thyroid is obtained by FNA, whether it is performed under ultrasound guidance or not, and also depends upon the experience in smearing and preparation of the cytology slides,
- b) the experience of the cytology technologists,



- c) The interpretation in case of cytologic material, particularly in lesions such as uncertain categories which include the follicular lesions, iv) and finally the reporting method of the thyroid FNA results.

Being a tertiary care hospital we receive many patients of thyroid disorders from the nearby districts. The majority of the lesions are usually benign and they require no aggressive treatment. The interpretation in each and every case is very crucial for further management. Also we wanted to have an uniform communication between the pathologist, radiologist, endocrinologist, surgeons and the treating physicians. So that there would be no confusion regarding the management of every patients.

To achieve the standardization in the reporting of thyroid FNA, the National Cancer Institute (NCI) hosted the 'NCI Thyroid Fine Needle Aspiration State of the Science Conference' which gave rise to the information of 'The Bethesda System for Reporting Thyroid Cytopathology' (TBSRTC) <sup>[89,90]</sup>. TBSRTC is a vital classification as it bridges the communication gap and is useful to maintain uniformity in the reporting of thyroid lesions. We followed the TBSRTC guidelines and each and every case was classified according to the six tier reporting guideline from category I to VI according to the Bethesda classification.

The use of these well-defined criteria for adequacy in thyroid FNA samples is helpful as they improve the diagnostic efficiency of thyroid FNA and also avoid the unnecessary surgery for benign and non neoplastic thyroid

lesions. The lesional characteristics of the thyroid gland and other than cystic features which cause sampling error are with the thyroid gland which presents with multiple nodules, calcification and fibrosis. The sample adequacy of the FNA thyroid may be affected by the structure of lesion and the needle localization ‘ the geographic miss of the needle’, the method of guidance, the number of aspirated samples, the needle gauge, the aspiration technique, and the presence or absence of on-site facilities for immediate cytologic examination.

The category of the ND/UNS cytologic findings may also result from factors such as poor preparation of the smear, poor fixation of the smear or poor staining or from the presence of excessive blood, presence of necrotic material, or debris obscuring cellular details, and also misinterpretations. However it is, important to keep in mind that ND/UNS specimen does not always mean as a negative specimen. An experienced cytopathologist, can do an accurate localization of the lesion either by palpation or by ultrasound, and by performing between 1-5 aspirates for thyroid nodules of 1-2 cms size with 20-27 gauge needles, using standard sampling technique, supported by immediate on-site cytological analysis can ensure specimen adequacy. The nodules which are reported as ND/UNS result should be re-aspirated, but no sooner than 3 months later; the 3-month interval is recommended so as to prevent the false positive interpretations due to reactive/reparative changes. The categories that require repeat FNA include the sample inadequacy,

nodule enlargement, cyst recurrence, or clinical or imaging findings that arouse a suspicion of a malignancy even when the cytological findings in the biopsy specimen indicate benignity. The thyroid FNA with an ultra sound guidance is preferred for a repeat aspiration in the case where an ND/UNS report has been given, and especially for solid nodules. The repeating of thyroid FNA results in a diagnostic interpretation in up to 60% of cases. Several studies have shown that the ultrasound guided FNAs of thyroid have shown to reduce the rates of non-diagnostic (i.e., insufficient cells and/or colloid) and the false negative aspirates.

A simplified reporting scheme would, undoubtedly, have to address the assessment of adequacy and an acceptable rate of inadequate diagnoses could then be determined <sup>[91]</sup>.

The reporting of thyroid cytology classification by using Bethesda System is a standardized reporting and it classifies the thyroid fine-needle aspiration reports into 6 diagnostic categories which have a unique risks of malignancy and have specific recommendations for clinical management. The categories include (I) Nondiagnostic (II) Benign (III) Atypia of undetermined significance /follicular lesion of undetermined significance (IV) Follicular neoplasm/suspicious for a follicular neoplasm (V) Suspiciously for malignancy and (VI) Malignant aspirates.<sup>[92,93,94]</sup> By using the Bethesda reporting system it helps in the better prognosis, management

as well as patient's outcome and it also minimizes the unwanted surgical procedures for thyroid swellings.<sup>[95]</sup>

The fine needle which was used in present study had a gauge of 23 and was found to yield good cellular smears. The length of the needle favoured was one and a half inches and in the present study the same was found to be of optimal length and reached all the areas in a thyroid nodule. 10 ml or 20 ml syringes were employed by most operators. Walfish et al. (1977) used 10 ml syringe fitted with an 18 gauge needle for cystic lesions. Thomas A Colacchio et al. (1980) used 5 ml syringe. 1 ml of tuberculin syringe with a 1.5 cm long 25 gauge needle mounted on it was employed by Norton LW et al. (1982). In our series a 5ml of disposable syringe was used and 10 ml of syringe used occasionally when the cystic fluid was aspirated.

All the authors used disposable needles including in the present study as they are least traumatic, less painful and perfectly sterile. A local anaesthetic was infiltrated into the skin to avoid pain to the patient by Colacchio TA et al. (1980), Norton W et al. (1982) and Rosen IB et al. (1981). None of the patients complained of significant pain in the present study. Local anaesthesia was not required according to the present study, when a fine and disposable needle (22- 24) gauge is used.<sup>[96] [97]</sup>

There were 3 unsatisfactory aspirations out of total 300 cases. They contained only haemorrhage and thin cystic fluid in the background admixed

with predominantly cyst macrophages and a very few scattered thyroid follicular epithelial cells.

### **SATISFACTORY SMEARS [TABLE -13]**

In our study of 300 cases, 297 aspirations were satisfactory and 3 aspirations were unsatisfactory as it contained only haemorrhage and thin cystic fluid in the background admixed with predominantly cyst macrophages and few inflammatory cells.

***TABLE- 13: Percentage of satisfactory smears from different series***

<b>SI NO</b>	<b>Name of the Author</b>	<b>year</b>	<b>Number of Aspirations</b>	<b>Adequate Material</b>	<b>Percentage</b>
1	Walfish et al. <sup>[101]</sup>	1977	88	83	94.3%
2	Frable and Frable <sup>[102]</sup>	1979	91	87	95.6%
3	Rosen LB et al <sup>[103]</sup>	1980	153	144	94. 0%
4	Al shayer HM et al <sup>[104]</sup>	1983	62	61	98.0 %
5	Klemi PJ et al <sup>[105]</sup>	1990	1054	1007	95.5%
6	Tabaqchali et al <sup>[106]</sup>	2000	302	210	70.02%
7	Sclabas GM et al <sup>[107]</sup>	2003	240	225	93.02%
8	<b>Present study</b>	<b>2013</b>	<b>300</b>	<b>297</b>	<b>99 .0%</b>



The above table shows the percentage and number of satisfactory aspirations in present study and in different series. Our study showed the highest number of satisfactory smears, followed by Al shayer HM et al.

### **AGE DISTRIBUTION**

The age of the patients varied from 9 to 85 years with the mean age of 38.3 years. The mean age group studied by Gershengorn et al (1977) was 39 years.. Colacchio TA et al (1980) reported the age of their patients ranging between 30 – 60 years. The age of the patients studied by Bhagat VM et al (2014) ranged from 20 – 50 years, the age group ranged from from 5 years to 70 years in this study. <sup>[98]</sup> The age of the patients studied by Silverman JF et al (1987) ranged from 16- 79 years.

In the present study, patients in the third and fourth decades of life comprised 68 %. Age distribution of lesions in our study correlates well with the observation of Bhagat V M et al (2014) with 67 % of cases in the third and fourth decade and the study of Pandit AA and Kinare et al (1986) who reported 62% cases in third and fourth decade.

### **GENDER DISTRIBUTION**

The gender ratio (female : male ) in the present study was 16.5 : 1. The majority of cases were females mostly encountered in the young and middle age groups. In the series of Bhagat VM et al (2014) female to male ratio was 5.67:1. <sup>[90]</sup> Pandit AA and Kinare et al (1986) reported female : male ratio was 58:26., Klemi PJ et al (1990) series, female: male ratio was

8:1. Similar female predominance seen in studies conducted by Unnikrishnan et al (2011).<sup>[98]</sup> High frequency of women were observed in the present study which correlated with most of the other series. We had a similar observation.

## **DISTRIBUTION OF LESIONS ACCORDING TO BETHESEDA CLASSIFICATION**

### **CATEGORY I - NON DIAGNOSTIC OR UNSATISFACTORY**

This category includes the cases in which the adequate material for reporting like six groups of well visualised thyroid follicular cells with at least minimum of ten cells per group is not present, or the prescence of cyst fluid only, or any obscuring elements like only macrophages or haemorrhage or any preparation artifact. In the present study out of the total 300 cases, 3 cases (1%) were present in this category as these smears did not have the adequate thyroid clusters, there were only few scattered thyroid follicular cells, and the smears contained only haemorrhage, admixed with a cystic fluid and predominant sheets of cyst macrophages and few inflammatory cells. The percentage of cases under this category were very less when compared to other studies as mentioned in TABLE -14 .<sup>[99]</sup>

**TABLE- 14 : Percentage of cases in Non – diagnostic category according to Bethesda in different series.**

S.NO	SERIES	NON-DIAGNOSTIC (%)
1.	Faquin WC in Krane J F et al (2011) <sup>[108]</sup>	13.9
2	Kim SK et al (2011) <sup>[109]</sup>	1.8
3.	Nayar R in Ivanovic et al (2009) <sup>[110]</sup>	5.3
4.	Theoharis CG et al (2009) <sup>[111]</sup>	11.1
5.	VanderLaan PA et al (2011) <sup>[112]</sup>	12.5
6.	Marchevsky AM (2010) et al <sup>[113]</sup>	12.9
7.	Jo V Y et al (2010) <sup>[114]</sup>	18.6
8.	Renshaw AA et al (2010) <sup>[115]</sup>	23.6
9.	<b>Present study</b>	<b>0.3</b>

The TABLE-14 shows the percentage of cases diagnosed in the Non-diagnostic category in the present study and in different series. In our present study the number of cases under this category were less compared to other series. Renshaw AA et al (2010) series showed a highest percentage of cases under this category followed by Faquin WC in Krane J F et al (2011) Marchevsky AM (2010) et al and VanderLaan PA et al (2011). Rest of the series showed a slight higher percentage of cases compared to our study.

## **CATEGORY II – BENIGN :**

The term benign follicular nodule is applied to most common benign pattern and the other subcategories under this benign lesions include hashimoto's thyroiditis, granulomatous (subacute ) thyroiditis.

In the present study out of the 300 cases 274 cases (91.3%) were diagnosed as benign lesions by classifying them in the Bethesda classification. The most common benign conditions that constitutes the group includes 131 cases of adenomatous goitre (43.7%), and followed by 90 cases of Hashimoto's thyroiditis, 52 cases of colloid rich nodule (17.3%) and a single case of granulomatous (subacute ) thyroiditis.

We had a higher percentage of cases under the category when compared with the observation of other authors. When comparing various studies it shows that the cases diagnosed under the benign category of Bethesda comprises the bulk of thyroid lesions compared with the other diagnostic categories in the Bethesda system of classification. In the studies conducted by Unnikrishnan et al (2011), Bhagat VM et al (2014) had similar findings and 60-70% cases belonged to benign category.<sup>[99]</sup> The other studies done by various authors showed various percentages under this category which are mentioned in TABLE-15.

**TABLE 15: Percentage of thyroid lesions in Benign category according to Bethesda in different series.**

S.NO	SERIES	BENIGN (%)
1.	Faquin WC in Krane J F et al (2011) <sup>[108]</sup>	66.9
2.	Kim SK et al (2011) <sup>[109]</sup>	58.3
3.	Nayar R in Ivanovic et al (2009) <sup>[110]</sup>	64.2
4.	Theoharis CG et al (2009) <sup>[111]</sup>	73.8
5.	VanderLaan PA et al (2011) <sup>[112]</sup>	62.7
6.	Marchevsky AM (2010) et al <sup>[113]</sup>	71.6
7.	Jo V Y et al (2010) <sup>[114]</sup>	59.0
8.	Renshaw AA et al (2010) <sup>[115]</sup>	54.0
9.	<b>Present study</b>	<b>91.3</b>

The TABLE-15 shows the percentage of cases diagnosed under benign category in present study and in different series. Our study showed the highest percentage of cases diagnosed under this category followed by Marchevsky AM et al and the rest of the series had a similar distribution of cases under this category.

### **CATEGORY III : ATYPIA OF UNDETERMINED SIGNIFICANCE OR FOLLICULAR LESION OF UNDETERMINED SIGNIFICANCE**

It includes the thyroid lesions that cannot be classified as benign, suspicious for malignancy or malignant lesions, an AUS result of (3- 6% ) is

obtained in a routine thyroid FNA, this category should be used very discriminately. In the present study 1 case (0.3%) was reported under this category. The other studies done by various authors showed various percentages under this category which are mentioned in TABLE-16.

**TABLE- 16: Percentage of cases in various studies in the AUS/FLUS category.**

S.NO	SERIES	AUS/ FLUS (%)
1.	Faquin WC in Krane JF et al (2011) <sup>[108]</sup>	10.0
2.	Kim SK et al(2011) <sup>[109]</sup>	16.3
3.	Nayar R in Ivanovic M et al (2009) <sup>[110]</sup>	17.8
4.	Theoharis CG et a <sup>[111]</sup>	3.0
5.	VanderLaan M et al <sup>[112]</sup>	10.9
6.	Marchevsky AM et al(2010) <sup>[113]</sup>	9.8
7.	Jo VY et al (2010) <sup>[114]</sup>	3.4
8.	Renshaw AA et al (2010) <sup>[115]</sup>	7.7
9.	Bhagat VM et al (2014) <sup>[18]</sup>	0
10.	<b>Present study</b>	<b>0.3</b>

The TABLE-16 shows the AUS percentages in present study and in different series, the AUS percentage in present study was very less compared to other studies except in the studies done by Bhagat VM et al (2014) reported nil case under this category, the highest percentage of cases under

this category was reported in the studies of Nayar R in Ivanovic M et al (2009).

#### **CATEGORY IV: FOLLICULAR NEOPLASM / SUSPICIOUS FOR FOLLICULAR NEOPLASM:**

The main aim of this category is to potentially identify all the follicular carcinomas and help in the proper management of these lesions and refer them for a surgical lobectomy. The cytomorphological features do not permit a clear cut distinction of a follicular adenoma from a follicular carcinoma, they are reported as follicular neoplasm or suspicious for follicular neoplasm, thus leading to a definitive management to the patients like usually lobectomy is carried out. The majority of the lesions reported under this category turn out to be a follicular adenoma or adenomatoid nodules of multinodular goiter, both of them are common and it usually outnumbers the lesions such as follicular carcinoma.

In the present study 12 cases (4%) were studied under this category. The other studies done by various authors showed various percentages under this category which are mentioned in the TABLE-17.<sup>[99]</sup>

**TABLE - 17: Percentage of thyroid lesions in FN/SFN category in different series.**

<b>S.NO</b>	<b>SERIES</b>	<b>FN/SFN (%)</b>
1.	Faquin WC in Krane J F et al (2011) <sup>[108]</sup>	2.0
2.	Kim SK et al (2011) <sup>[109]</sup>	1.2
3.	Nayar R in Ivanovic et al (2009) <sup>[110]</sup>	5.9
4.	Theoharis CG et al (2009) <sup>[111]</sup>	5.5
5.	VanderLaan PA et al (2011) <sup>[112]</sup>	4.2
6.	Marchevsky AM (2010) et al <sup>[113]</sup>	1.5
7.	Jo V Y et al (2010) <sup>[114]</sup>	9.7
8.	Renshaw AA et al (2010) <sup>[115]</sup>	8.6
9.	<b>Present study</b>	<b>4.0</b>

The TABLE-17 shows the percentage of Follicular neoplasm / Suspicious for follicular neoplasm cases in present study and in different series. Our study showed 4% of cases diagnosed under this category which were similar with the studies done by VanderLaan PA et al (2011). The highest number of cases were reported in the series of Nayar R in Ivanovic et al (2009). The other series showed less number of cases diagnosed under this category compared to our study. Kim SK et al (2011) series reported least number of cases under this category.



## **CATEGORY V : SUSPICIOUS FOR MALIGNANCY :**

This category includes the lesions that in which the nuclear and architectural features are very subtle to classify them as malignant, so they are best classified as suspicious for malignancy, the lesions like follicular variant of papillary carcinoma the nuclear features are so subtle sometimes so that it becomes difficult to distinguish it from the benign follicular nodule. If only few characteristic features of papillary thyroid carcinoma are present, in a very sparsely cellular sample, a definite diagnosis of malignancy is not possible and such lesions are best classified under this category as suspicious for malignancy.

In the present study 2 cases were present under this category showing a percentage of 0.7%, the other studies conducted by various authors Showed various distributions of lesions under this category which are mentioned in (TABLE -18 ).

***TABLE- 18: Percentage of thyroid lesions in SFM category in different series.***

<b>S.NO</b>	<b>SERIES</b>	<b>SFM (%)</b>
1.	Faquin WC in Krane J F et al (2011) <sup>[108]</sup>	3.2
2.	Kim SK et al (2011) <sup>[109]</sup>	6.2
3.	Nayar R in Ivanovic et al (2009) <sup>[110]</sup>	1.9
4.	Theoharis CG et al (2009) <sup>[111]</sup>	1.3
5.	VanderLaan PA et al (2011) <sup>[112]</sup>	4.5
6.	Marchevsky AM (2010) et al <sup>[113]</sup>	2.3
7.	Jo V Y et al (2010) <sup>[114]</sup>	2.3
8.	Renshaw AA et al (2010) <sup>[115]</sup>	1.8
9.	<b>Present study</b>	<b>0.7</b>

The TABLE-18 shows the percentage of cases in the suspicious for malignancy category in present study and in different series. In this study the number of cases reported under this category were less compared to other studies. The studies done by Kim SK et al (2011) showed the highest number of cases under this category followed by the series of VanderLaan PA et al (2011) . Other series reportedly had average number of cases diagnosed under this category.

#### **CATEGORY VI : MALIGNANT**

This category is used when the cytological and nuclear features are indicative of a clear cut malignancy. Approximately 6-7% of thyroid FNAs have conclusive evidence of malignancy. And most of the malignant lesions usually are papillary carcinoma in type. Malignant lesions are usually treated by total thyroidectomy.

In the present study 8 cases(2.7%) out of 300 patients were diagnosed as malignant all of them showed features of papillary carcinoma. The studies done Bhagat V M et al (2014) reported 11 cases (6.88%) of neoplastic lesions. In the series of Mufti ST et al the malignant lesions included 8 cases (3.6%). The malignant lesions studied by different authors under Bethesda system shows the percentage of malignant lesions in thyroid which are mentioned in [TABLE – 19 ].

**TABLE – 19 : Percentage of thyroid lesions in malignant category according to Bethesda classification in different series.**

S.NO	SERIES	MALIGNANT (%)
1.	Faquin WC in Krane J F et al (2011) <sup>[108]</sup>	3.9
2.	Kim SK et al (2011) <sup>[109]</sup>	16.2
3.	Nayar R in Ivanovic et al (2009) <sup>[110]</sup>	4.9
4.	Theoharis CG et al (2009) <sup>[111]</sup>	5.2
5.	VanderLaan PA et al (2011) <sup>[112]</sup>	5.2
6.	Marchevsky AM (2010) et al <sup>[113]</sup>	2.0
7.	Jo V Y et al (2010) <sup>[114]</sup>	7.0
8.	Renshaw AA et al (2010) <sup>[115]</sup>	4.2
9.	<b>Present study</b>	<b>2.7</b>

The TABLE- 19 shows the percentage of cases diagnosed under the category of malignant lesions according to Bethesda in present study and in different series. Kim SK et al (2011) series had the highest number of cases diagnosed under this category followed by the series of Jo V Y et al (2010). The percentage of cases in our study correlated with the series done by Marchevsky AM (2010) et al. Other series showed a slight higher percentage of cases under this category compared to our present study.

**COMPARISON OF FNA DIAGNOSES BETWEEN THE PRESENT STUDY AND THE PUBLISHED VALUES IN OTHER STUDIES, EXPRESSED AS A PERCENTAGE OF ALL FNAs<sup>[100]</sup>**

***TABLE- 20 : Percentage of thyroid lesions according to Bethesda in present study and various other studies.***

<b>FNA Diagnoses</b>	<b>Present study N=300</b>	<b>Williams et al 2006<sup>[116]</sup> N=1491</b>	<b>Yang et al., 2007<sup>[117]</sup> N = 4703</b>	<b>Jo et al., 2010<sup>[118]</sup> N=3080</b>	<b>Wu et al.2011<sup>[119]</sup> N=1382</b>
ND	1%	28.9%	10.4%	18.6%	20.1%
BENIGN	91.3%	45.7%	64.6%	59.0%	39.0%
AUS/FLUS	0.3%	18.8%	3.2%	3.4%	27.2%
FN/SFN	4%	4.4%	11.6%	9.7%	8.4%
SFM	0.7%	1.3%	2.6%	2.3%	2.6%
MALIGNANT	2.7%	0.9%	7.6%	7.0%	2.7%

The TABLE -20 shows the comparison of thyroid lesions classified under Bethesda in present study and in different series. The benign lesions comprised of highest number of cases in present study compared to all other studies, other studies also showed highest number of cases in benign category compared to other categories. In the present study AUS category showed the least number of cases compared to other studies. The cases in the SFN/FN category were similar with the studies of William et al as shown in

[TABLE – 20], other studies showed higher number of cases. In the present study the cases in the SFM category were also comparable with Williams et al <sup>[100]</sup>, other studies showed higher number of cases. The cases in the malignant category were similar as that studied by Wu et al, whereas Williams et al reported a least number of cases under this category, other studies showed a slight higher percentage.

These data demonstrate that the Bethesda system is excellent for reporting thyroid FNAs. Each diagnostic category conveys specific risks of malignancy and offers appropriate guidance for patient's management.

## **SUMMARY**

A prospective study of fine needle aspiration cytology of nodular and diffuse lesions of thyroid was carried out and the cytomorphology of these lesions were studied and reported with emphasis on Bethesda system of reporting, during the period from January 2013 to June 2014 in the Cytopathology laboratory of the Department of Pathology, Tirunelveli Medical College, Tirunelveli

The findings in the present study can be summarised as follows:

- FNAC was performed on 300 cases for cytological evaluation of the thyroid lesions and classifying them in Bethesda.
- Out of the total aspirations 3 cases were unsatisfactory aspirations. Age of the patients ranged from 9 – 85 years of age. The youngest patient was a 9 year old female and the oldest was an 85 year old female.
- Females formed the predominant group comprising of 283 cases (94.3%) out of the total 300 cases.
- Majority of the patients in the present study were in the third to fourth decade of life.
- Of the total 300 cases, the majority of the cases were benign (91.3%)

- Among the malignancies, all of them were papillary carcinomas(100%)
- The cytomorphological profile of nodular and diffuse thyroid lesions were classified by Bethesda as non diagnostic, benign, atypia of undetermined significance/ follicular lesion of undetermined significance, follicular neoplasm / suspicious for follicular neoplasm, suspicious for malignancy and malignant categories.
- Out of the total 300 cases highest number of cases occurred in category II benign comprising of 274 cases (91.3% ), Non – diagnostic category comprising of 3 cases (1%), under the category of Atypia of undetermined significance / Follicular lesion of undetermined 1 case (0.3%) was reported, and under the category of Suspicious of malignancy 2 cases(0.7%) were reported.
- Under the category of malignant lesions 8 cases (2.7%) were reported and all of them were papillary carcinoma of thyroid.

## CONCLUSION

- FNAC is simpler, safer, quicker and more informative compared to other sophisticated investigations in the diagnosis of thyroid lesions.
- When there is a marked cellularity of the smear it is an inherent problem in thyroid FNAC. Increased cellularity of the smear and loss of cohesion may be present in hyperplastic/adenomatous goiter and follicular neoplasm which causes difficulty in differentiating them. This can be solved by using the Bethesda System of Reporting thyroid lesions.
- The Bethesda system for reporting thyroid cytology plays an essential role in establishing the uniform communications between the managing medical personnel.
- The Bethesda system of reporting thyroid cytology is a vital guide in the accurate management of thyroid lesions.
- Thus we conclude that by using the Bethesda reporting system in thyroid cytology it helps in the prognosis, management and in the patient's outcome and also minimizes the unnecessary surgical procedures for thyroid swellings.



## **BIBLIOGRAPHY :**

1. Christopher D. M. Fletcher. Diagnostic Histopathology of tumors. Vol 2,3<sup>rd</sup> ed, Elsevier, Thyroid gland. 2007;997-1080.
2. Koss LG,Diagnostic cytology and its histopathologic basis. Vol 2, 4<sup>th</sup> ed, New York, J B Lipincott, 1992 ; 1268 -1279.
3. Accuracy of Fine Needle Aspiration of Thyroid. A review of 6226 cases and correlation with surgical and clinical outcome. Mojghan Amvikachi MN, Ibrahim Ramzy MD ; Sheldon Rubenfeld. MD et
4. Vnder J B, Gaston EA,Dawber T R. The significance of non-toxic thyroid nodules ; final report of a 15 year study of the incidence of thyroid malignancy. Ann Int Med. 1968;69;537-540.
5. Gharib H.Fine Needle Aspiration biopsy of thyroid ; an appraisal ;Ann Int Med 1993;118;282-289.
6. Rojeski MT, Gharib H.Nodular thyroid disease ;Evaluation and management,N Engl J med. 1985 ;313: 428-436.
7. Yuri. E Nikiforov. Thyroid tumors ; Classification, staging and general consideration. Longo, hematology Ch 45; 569-577.
8. Burnicardi FC, Anderson D K, Billiar TR, Dunn DL, Hunter JF, Mathew JB, Pollock RE, Schwartz;s Principles of surgery,9<sup>th</sup> edition.
9. Henry J F, Surgical anatomy and embryology of the thyroid and parathyroid glands and recurrent and external laryngeal nerves. In

- ;Clark OH, Duli QY (ed), Text book of endocrine surgery. Philadelphia;WB Saunders 1997 ;8-14.
- 10.Rosai & Ackerman's Textbook of surgical Pathology, 10<sup>th</sup> ed. New York. Elsevier. Thyroid gland. 2011.
  - 11.De Felice M, Di Hauo R : Thyroid development and its disorders : genetics and molecular mechanism. Endocr Rev 2004; 25: 722- 746.
  - 12.Livolvi VA, The thyroid Physiology. In Text book of endocrine surgery, Clark OH,Dal QY (eds) Philadelphia ; WA Saunders ;1997;3(1).
  - 13.Virgina A. Livolsi. Surgical pathology of the thyroid. Major problems in pathology. Vol22. Philadelphia WB saunders 1990;365 : 649-51
  - 14.Ben-Ezra J, Wu A, Sheibani K: Hashimoto's thyroiditis lacks detectable clonal immunoglobulin and T cell receptor gene rearrangements. Hum Pathol 1988; 19:1444-1448.
  - 15.Carcangiu M L, Debellis RA, Thyroid gland, Damjanov,Linder J,editors Andersons Pathology, 10<sup>th</sup>ed St Louis Morby,1996;1943-1972
  - 16.Jayaram G, Singh B, Marwaha RK.Graves' disease. Appearance in cytologic smears from fine needle aspirates of the thyroid gland. Acta Cytol 1989;33:36–40.

17. Ronald A. De lellis E.D Williams. WHO classification of tumors, Pathology and genetics. Tumours of endocrine organs. Edited by, IARC, Lyon, 2004.
18. Bhagat VM, Hemali J. Tailor, Kumar Bhargav R. Kaptan,. Varsha Baladawa, Gunjan H. Prasad,. Peeyush K. Diagnostic Role of the Bethesda System for Reporting Thyroid Lesions: Effective Tool for Managing Thyroid Lesions Volume 14 Issue 1 Version 1.0 Year 2014
19. Orell SR, Sterett OF, Waiter MN, Whitaler D, editors, the thyroid gland. In Manual and Atlas of fine needle aspiration cytology, 3<sup>rd</sup> ed, London, Chrchill, Livingstone, 1999, 109-144.
20. Biboo M. Comprehensive Cytopathology, 2<sup>nd</sup> ed, Chicago, WB Saunder, 1997; 673-701.
21. Schmid KW, Ladurner D, Zechmann W, et al. Clinicopathologic management of tumours of the thyroid gland in an endemic goitre area. Combined use of preoperative fine needle aspiration biopsy and intraoperative frozen section. Acta Cytol 1989; 33: 27–30.
22. Muruganandham K, Sistla SC, Elangovan S. et al. Routine ultrasound guided aspiration cytology for evaluation of palpable thyroid nodules in an endemic area: is it justified? J Otolaryngol Head Neck Surg 2009; 38: 222–6.
23. Sanjos J, Leiman G, Non-aspiration fine needle cytology. Acta cytological 1998; 32: 353-356.

24. Orell SR, Strett OF, Waiter MN, Whittaker D editors, the thyroid gland. In Manual and Atlas of fine needle aspiration cytology, 3rd ed, London, Churchill, Livingstone, 1999
25. Stanley MW, Lowhagen T. Fine needle aspiration of palpable masses. Boston : Butterworth- Heinemann; 1993.
26. Kini SR, Miller J M, Hamsurger J. Smith - Purslove MJ. Cytopathological features of follicular lesion of thyroid. Diag Cytopathol 1985 ; 1: 123-32.
27. Kini SR, Post – Fine needle biopsy infarction of thyroid neoplasm. A review of 28 cases. Diag cytopathol 1996; 15: 211- 20.
28. Roussel F, Dalin J, Benizio M. The risk of tumor seeding in needle biopsies. Acts Cytol 1989 ; 33: 96- 9.
29. Powers C N. Complications of FNAB: the reality behind myths. In Cytopathology, Schmidt WA, ed. Chicago: ASCP press, 1996; P.69-91.
30. Ali SZ, Cibas ES. The Bethesda System for Reporting Thyroid Cytopathology. New York, NY: Springer. In press.
31. Baloch ZW, LiVolsi VA, Asa SL, et al. Diagnostic terminology and morphologic criteria for cytologic diagnosis of thyroid lesions: a synopsis of the National Cancer Institute Thyroid Fine-Needle Aspiration State of the Science Conference. Diagn Cytopathol. 2008;36(6):425-437(1)

32. Clark DP, Faquin WC. Thyroid Cytopathology. New York: Springer; 2005.
33. Berezowski K, Jovanovic I, Sidawy MK. Thyroid. In: Sidawy MK, Ali SZ, eds. Fine Needle Aspiration Cytology. Churchill:Livingstone 2007 [Chapter2].
34. Elsheikh TM, Singh HK, Saad R, Silverman JF. Fine needle aspiration of the head and neck. In: Barnes L, ed. Surgical pathology of the head and neck. New York:Informa Healthcare USA 2009
35. Orell SR, Philips J. The Thyroid. Fine needle biopsy and cytological diagnosis of thyroid lesions. Vols. 14. Basel:Kaarger 1997
36. Soderstrom N, Nilsson G. Cytologic diagnosis of thyrotoxicosis. Acta Med Scand. 1979;205(4):263-265.
37. Jayaram G, Marwaha RK, Gupta RK, Sharma SK. Cytomorphologic aspects of thyroiditis. A study of 51 cases with functional, immunologic and ultrasonographic data. Acta Cytol 1987;31(6):687–693.
38. Pitman MB, Abele J, Ali S, et al. Techniques for Thyroid FNA: a synopsis of the national cancer institute thyroid fine needle aspiration state of the science conference. Diagn Cytopathol. 2008;36(6):407-424.

- 39.Lu CP, Chang TC, Wang CY, Hsiao YL. Serial changes in ultrasound-guided fine needle aspiration cytology in subacute thyroiditis. *Acta Cytol.* 1997;41(2):238-243.
- 40.Syed Z. Ali and Edmund S. Cibas (eds.), *The Bethesda System for Reporting Thyroid Cytopathology*, DOI 10.1007/978-0-387-87666-5\_4,
- 41.Nayar R, Ivanovic M. The indeterminate thyroid FNA: Experience from an academic center using terminology similar to that proposed in the 2007 NCI Thyroid Fine Needle Aspiration State of the Science Conference. *Cancer Cytopathol* 2009;117:195–202.
- 42.Yassa L, Cibas ES, Benson CB, et al. Long-term assessment of a multidisciplinary approach to thyroid nodule diagnostic evaluation. *Cancer.* 2007;111(6):508-516.
- 43.Renshaw AA, Wang E, Wilbur D, Hughes JH, Haja J, Henry MR. Interobserver agreement on microfollicles in thyroid fine-needle aspirates. *Arch Pathol Lab Med.* 2006;130(2):148-52.
- 44.Elsheikh TM, Asa SL, Chan JK, et al. Interobserver and intraobserver variation among experts in the diagnosis of thyroid follicular lesions with borderline nuclear features of papillary carcinoma. *Am J Clin Pathol.* 2008;130(5):736-44.
- 45.Hurthle K. A study of the secretory process of the thyroid gland. *Arch F D Ges Physiol.* 1894:56.

46. Askanazy M. Pathologisch-anatomische beitrage zure kenntnis des morbus basedowii, insbesondere uber die dabei auftretende muskelerkrankung. Dtsch Arch Klin Med. 1898;61:118
- 47.14. Kini SR, Miller JM, Hamburger JI. Cytopathology of Hurthle cell lesions of the thyroid gland by fine needle aspiration. Acta Cytol. 1981;25(6):647-652.
48. Nguyen GK, Husain M, Akin MR. Cytodiagnosis of benign and malignant Hurthle cell lesions of the thyroid by fine-needle aspiration biopsy. Diagn Cytopathol. 1999;20(5):261-265.
49. Wu HH, Clouse J, Ren R. Fine-needle aspiration cytology of Hurthle cell carcinoma of the thyroid. Diagn Cytopathol. 2008;36(3):149-154.
50. Elliott DD, Pitman MB, Bloom L, et al. Fine-needle aspiration biopsy of Hurthle cell lesions of the thyroid gland: a cytomorphologic study of 139 cases with statistical analysis. Cancer. 2006;108(2):102-109.
51. Wang HH. Reporting thyroid fine-needle aspiration: Literature review and a proposal. Diagn Cytopathol. 2006;34(1):67-76
52. Granter SR, Cibas ES. Cytologic findings in thyroid nodules after 131iodine treatment of hyperthyroidism. Am J Clin Pathol. 1997;107:20-25.
53. Centeno BA, Szyfelbein WM, Daniels GH, Vickery AL. Fine-needle aspiration biopsy of the thyroid gland in patients with prior Graves'

- disease treated with radioactive iodine: morphologic findings and potential pitfalls. *Acta Cytol.* 1996;40:1189-1197.
54. Zhang Y, Fraser JL, Wang HH. Morphologic predictors of papillary carcinoma on fineneedle aspiration of thyroid with ThinPrep preparations. *Diagn Cytopathol.* 2001;24(6):378-383.
55. Liu J, Singh B, Tallini G, et al. Follicular variant of papillary thyroid carcinoma: a clinicopathologic study of a problematic entity. *Cancer.* 2006;107(6):1255-1264.
56. Das DK, Mallik MK, Sharma P, et al. Papillary thyroid carcinoma and its variants in fine needle aspiration smears A cytomorphologic study with special reference to tall cell variant. *Acta Cytol.* 2004;48(3):325-336.
57. Gupta S, Sodhani P, Jain S, Kumar N. Morphologic spectrum of papillary carcinoma of the thyroid: role of cytology in identifying the variants. *Acta Cytol.* 2004;48(6):795-800.
58. Ylagan LR, Dehner LP, Huettner PC, Lu D. Columnar cell variant of papillary thyroid carcinoma Report of a case with cytologic findings. *Acta Cytol.* 2004;48(1):73-77.
59. Goellner JR, Johnson DA. Cytology of cystic papillary carcinoma of the thyroid. *Acta Cytol.* 1982;26(6):797-808.



60. Lloyd RV, Erickson LA, Casey MB, et al. Observer variation in the diagnosis of follicular variant of papillary thyroid carcinoma. *Am J Surg Pathol.* 2004;28(10):1336-1340.
61. Rosai J, Zampi G, Carcangiu ML. Papillary carcinoma of the thyroid. A discussion of its several morphologic expressions, with particular emphasis on the follicular variant. *Am J Surg Pathol.* 1983;7(8):809-817.
62. Carcangiu ML, Zampi G, Pupi A, Castagnoli A, Rosai J. Papillary carcinoma of the thyroid. A clinicopathologic study of 241 cases treated at the University of Florence, Italy. *Cancer.* 1985;55(4):805-828.
63. Baloch ZW, Gupta PK, Yu GH, Sack MJ, LiVolsi VA. Follicular variant of papillary carcinoma. Cytologic and histologic correlation. *Am J Clin Pathol.* 1999;111(2):216-222.
64. Fulciniti F, Benincasa G, Vetrani A, Palombini L. Follicular variant of papillary carcinoma: cytologic findings on FNAB samples-experience with 16 cases. *Diagn Cytopathol.* 2001;25(2):86-93.
65. Goodell WM, Saboorian MH, Ashfaq R. Fine-needle aspiration diagnosis of the follicular variant of papillary carcinoma. *Cancer.* 1998;84(6):349-354.
66. Mesonero CE, Jugle JE, Wilbur DC, Nayar R. Fine-needle aspiration of the macrofollicular and microfollicular subtypes of the follicular

- variant of papillary carcinoma of the thyroid. *Cancer*. 1998;84(4):235-244.
67. Chung D, Ghossein RA, Lin O. Macrofollicular variant of papillary carcinoma: a potential thyroid FNA pitfall. *Diagn Cytopathol*. 2007;35(9):560-564.
68. Goellner JR, Johnson DA. Cytology of cystic papillary carcinoma of the thyroid. *Acta Cytol*. 1982;26(6):797-808.
69. Faquin WC, Cibas ES, Renshaw AA. "Atypical" cells in fine-needle aspiration biopsy specimens of benign thyroid cysts. *Cancer*. 2005;105(2):71.
70. Moreira AL, Waisman J, Cangiarella JF. Aspiration cytology of the oncocytic variant of papillary adenocarcinoma of the thyroid gland. *Acta Cytol*. 2004;48(2):137-141.
71. Doria MI Jr, Attal H, Wang HH, Jensen JA, DeMay RM. Fine needle aspiration cytology of the oxyphil variant of papillary carcinoma of the thyroid. A report of three cases. *Acta Cytol*. 1996;40(5):1007-1011.
72. Baloch ZW, LiVolsi VA. Warthin-like papillary carcinoma of the thyroid. *Arch Pathol Lab Med*. 2000;124(8):1192-1195.
73. Ghossein RA, LiVolsi VA. Papillary carcinoma, tall cell variant. *Thyroid*. 2008;18(11):1179-1181.
74. Solomon A, Gupta PK, LiVolsi VA, Baloch ZW. Distinguishing tall cell variant of papillary thyroid carcinoma from usual variant of

- papillary thyroid carcinoma in cytologic specimens. *Diagn Cytopathol.* 2002;27(3):143-148.
75. Jayaram G. Cytology of columnar-cell variant of papillary thyroid carcinoma. *Diagn Cytopathol.* 2000;22(4):227-229.
76. Goellner JR, Carney JA. Cytologic features of fine needle aspirates of hyalinizing trabecular adenoma of the thyroid. *Am J Clin Pathol.* 1989;91:115-119.
77. Casey MB, Sebo TJ, Carney JA. Hyalinizing trabecular adenoma of the thyroid gland: cytologic features in 29 cases. *Am J Surg Pathol.* 2004;28(7):859-867.
78. Forrest CH, Frost FA, de Boer WB, et al. Medullary carcinoma of the thyroid: accuracy of diagnosis of fine-needle aspiration cytology. *Cancer.* 1998;84(5):295-302.
79. Hsieh MH, Hsiao YL, Chang TC. Fine needle aspiration cytology stained with Rius method in quicker diagnosis of medullary thyroid carcinoma. *J Formos Med Assoc.* 2007;106(9):728-735
80. Sobrinho Simoes M, Albores-Saavedra J, Tallini G, et al. Poorly differentiated carcinoma. In: DeLellis R, Lloyd RV, Heitz PU, Eng C, eds. *World Health Organization Classification of Tumours: Pathology and Genetics of Tumours of Endocrine Organs.* Lyon: IARC Press 2004.

81. Volante M, Landolfi S, Chiusa L, et al. Poorly differentiated carcinomas of the thyroid with trabecular, insular, and solid patterns: a clinicopathologic study of 183 patients. *Cancer*. 2004;100(5):950-957.
82. Lehur PA, Cote RA, Poisson J, Boctor M, Elhilali M, Kandalaft N. Thyroid metastasis of clear-cell renal carcinoma. *Can Med Assoc J*. 1983;128(2):154-156
83. Agarwal S, Rao RS, Parikh DM, et al. Histologic trends in thyroid cancer 1969–1993: a clinico-pathologic analysis of the relative proportion of anaplastic carcinoma of the thyroid. *J Surg Oncol*. 1996;63(4):251-255.
84. Layfield LJ, Ostrzega N. Fine needle aspirate smear morphology in metastatic melanoma. *Acta Cytol*. 1989;33(5):606-612.
85. Sangalli G, Serio G, Zampatti C, Lomuscio G, Colombo L. Fine needle aspiration cytology of primary lymphoma of the thyroid: a report of 17 cases. *Cytopathology*. 2001;12(4): 257-263.
86. Murphy BA, Meda BA, Buss DH, Geisinger KR. Marginal zone and mantle cell lymphomas: assessment of cytomorphology in subtyping small B-cell lymphomas. *Diagn Cytopathol*. 2003;28(3):126-130.
87. Al-Marzooq YM, Chopra R, Younis M, Al-Mulhim AS, Al-Mommatten MI, Al-Omran SH. Thyroid low-grade B-cell lymphoma (MALT type) with extreme plasmacytic differentiation: report of a case

- diagnosed by fine-needle aspiration and flow cytometric study. *Diagn Cytopathol*. 2004;31(1):52-56.
- 88.Caruso D, Mazzaferri EL. Fine needle aspiration biopsy in the management of thyroid nodules.*Endocrinologist* 1. 1991: 194-202
- 89.NCI Thyroid Fine Needle Aspiration State of Science Conference. *Diagn Cytopathol*. 2008; 6:388-448.
- 90.Cochand-Priollet B, Schmitt FC, Totsch M, Vielh. The Bethesda terminology for reporting thyroid cytopathology: from theory to practice in Europe. *Acta Cytologica*. 2011;55:507-11
- 91.Bukhari MH, Niazi S, Hanif G, Qureshi SS, Munir M, et al. (2008) An updated audit of fine needle aspiration cytology procedure of solitary thyroid nodule. *Diagn Cytopathol* 36: 104-112.
- 92.Poller DN, Stelow EB, Yiangou C (2008) Thyroid FNAC cytology: can we do it better? *Cytopathology* 19: 4-10.
- 93.Basharat R, Bukhari MH, Saeed S, Hamid T (2011) Comparison of fine needle aspiration cytology and thyroid scan in solitary thyroid nodule. *Patholog Res Int* 2011: 754041.
- 94.Bongiovanni M, Spitale A, Faquin WC, Mazzucchelli L, Baloch ZW (2012) The Bethesda System for Reporting Thyroid Cytopathology: a meta-analysis. *Acta Cytol* 56: 333-339.

95. Cibas ES, Ali SZ, Conference NCITFSotS (2009) The Bethesda System For Reporting Thyroid Cytopathology. *Am J Clin Pathol* 132: 658-665.
96. Norton LW, Wangenstein SL, Davis JR, Paplamos SH, Werner SC. Utility of thyroid aspiration biopsy. *Surgery* 1982; 92: 700-5
97. Robinson IA, Cozens NJ. Does a joint ultrasound guided cytology clinic optimize the cytological evaluation of head and neck masses? *Clin Radiol* 1999; 54:312-6.
98. Unnikrishnan et al: Endocrine Society of India management guidelines for patients with thyroid nodules: A position statement, *Indian J Endol Metab.* 2011 Jan-Mar; 15(1): 2–8.
99. Paul A. VanderLaan, MD, PhD,<sup>1</sup> Andrew A. Renshaw, MD,<sup>2</sup> and Jeffrey F. Krane, MD, PhD<sup>1</sup> Anatomic Pathology / AUS and ND in TBS Are Inversely Related DOI: 10.1309/AJCPI41QOQUSKDGP
100. Williams et al. *Journal of Otolaryngology - Head and Neck Surgery* 2013, 42:61.
101. Walfish PG, Hazani E, Strawbridge HTG, Miskin M & Rosen IB 1977 Combined ultrasound and needle aspiration cytology in the assessment and management of hypofunctioning thyroid nodule. *Annals of Internal Medicine* 87 270-274.
102. Frable MA, Frable WJ. Thin needle aspiration biopsy of the thyroid gland. *Laryngoscope.* 1980;90:1619-1625.

103. Rosen IB, Wallace C, Strawbridge HG, Walfish PG. Revaluation of needle aspiration cytology in detection of thyroid cancer. *Surgery* 1981;90:747-756
104. Al-Sayer H, Krukowski ZH, Williams VMM, Mateson NA. Fine needle aspiration cytology in isolated thyroid swellings: a prospective two year evaluation. *Br Med J* 1985;290: 1490- 1492.
105. Klemi, PJ., Joensuu, H. and Nylamo, E. 1991. Fine Needle Aspiration biopsy in the diagnosis of thyroid nodules. *Acta Cytol.*; 35:35-8.
106. M. A. Tabaqchali, J. M. Hanson, S. J. Johnson, V. Wadehra, T. W. Lennard, and G. Proud. Thyroid aspiration cytology a six year cytology/histology correlation study. *Ann R Coll Surg Engl.* May 2000; 82(3): 149-155.
107. Sclabas GM<sup>1</sup>, Staerke GA, Shapiro SE, Fornage BD, Sherman SI, Vassilopoulou-Sellin R, Lee JE, Evans DB. Fine-needle aspiration of the thyroid and correlation with histopathology in a contemporary series of 240 patients. *Am J Surg.* 2003 Dec;186(6):702-9; discussion 709-10.
108. Krane JF, VanderLaan PA, Faquin WC, et al. The atypia of undetermined significance/follicular lesion of undetermined significance: malignant ratio: a proposed performance measure for reporting in The Bethesda System for Thyroid Cytopathology

[published online ahead of print September 14, 2011]. *Cancer Cytopathol.* In press. doi:10.1002/cncy.20192.

109. Kim SK, Hwang TS, Yoo YB, et al. Surgical results of thyroid nodules according to a management guideline based on the BRAFV600E mutation status. *J Clin Endocrinol Metab.* 2011;96:658-664.
110. Nayar R, Ivanovic M. The indeterminate thyroid fine needle aspiration: experience from an academic center using terminology similar to that proposed in the 2007 National Cancer Institute Thyroid Fine Needle Aspiration State of the Science Conference. *Cancer Cytopathol.* 2009;117:195-202.
111. Theoharis CG, Schofield KM, Hammers L, et al. The Bethesda thyroid fine-needle aspiration classification system: year 1 at an academic institution. *Thyroid.* 2009;19:1215- 1223.
112. VanderLaan PA, Marqusee E, Krane JF. Clinical outcome for atypia of undetermined significance in thyroid fine-needle aspirations: should repeated FNA be the preferred initial approach? *Am J Clin Pathol.* 2011;135:770-775.
113. Marchevsky AM, Walts AE, Bose S, et al. Evidence-based valuation of the risks of malignancy predicted by thyroid fineneedle aspiration biopsies. *Diagn Cytopathol.* 2010;38:252- 259.



114. Jo VY, Stelow EB, Dustin SM, et al. Malignancy risk for fine-needle aspiration of thyroid lesions according to The Bethesda System for Reporting Thyroid Cytopathology. *Am J Clin Pathol*. 2010;134:450-456.
115. Renshaw AA. Should “atypical follicular cells” in thyroid fine-needle aspirates be subclassified? *Cancer Cytopathol*. 2010;118:186-189.
116. Williams et al. Journal of Otolaryngology - Head and Neck Surgery 2013, 42:61
117. Yang J, Schnadig V, Logrono R, Wasserman PG: Fine-needle aspiration of thyroid nodules: a study of 4703 patients with histologic and clinical correlations. *Cancer* 2007, 111:306–315.
118. Jo VY, Stelow EB, Dustin SM, Hanley KZ: Malignancy risk for fine-needle aspiration of thyroid lesions according to the Bethesda system for reporting thyroid cytopathology. *Am J Clin Pathol* 2010, 134:450–456.
119. Wu HH-J, Rose C, Elsheikh TM: The Bethesda system for reporting thyroid cytopathology: an experience of 1,382 cases in a community practice setting with the implication for risk of neoplasm and risk of malignancy. *Diagn Cytopathol* 2012, 40:399–403.

**APPENDIX - I**  
**INFORMED CONSENT FORM**

**Study Title : Cytomorphological Evaluation Of Nodular And Diffuse Thyromegaly With Emphasis On Bethesda System Of Reporting – A Prospective Study.**

**Study Number** \_\_\_\_\_

**Subject's Full Name** \_\_\_\_\_

**Date of Birth/Age** \_\_\_\_\_

**Address**

\_\_\_\_\_  
\_\_\_\_\_

1. I confirm that I have read and understood the information sheet dated for the above study and have had the opportunity to ask questions. **or** I have been explained the nature of the study by the Investigator and had the opportunity to ask questions
2. I understand that my participation in the study is voluntary and that I am free to withdraw at anytime, without giving any reason and without my medical care or legal rights being affected.
3. I understand that the sponsor of the clinical trial/project, others working on the Sponsor's behalf, the Ethics Committee and the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the trial. However, I understand that my Identity will not be revealed in any information released to third parties or published.
4. I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s)
5. I agree to take part in the above study

**Signature (or Thumb impression) of the Subject/Legally Acceptable Representative:** \_\_\_\_\_

**Signatory's Name** \_\_\_\_\_

**Date** \_\_\_\_\_

**Signature of the Investigator** \_\_\_\_\_

**Date** \_\_\_\_\_

**Study Investigator's Name** \_\_\_\_\_

**Signature of the Witness** \_\_\_\_\_

**Date** \_\_\_\_\_

**Name of the Witness**

NehahspF S fF mwptpg kwWk; xgGj y; gbt k;

kUj ; J t Matpy; gqNfwgj wF

Ma;T nraaggLk; j i ygG : KbrRU kwWk; gut yhd i j uhaL Ruggpapd;  
capuZ mi kggpay; kj pgg i l ngj ] i h  
Ki wapd; %yk; typAWj ; k; mwptf f. Xh;  
tUqfhy Ma;T.

gqF ngWgthpd; ngah; :

gqF ngWgthpd; taJ :

		gqF ngWgth; , j i d FwptfTk;
1.	ehd; NkNy Fwpggl Lss kUj ; J Matpd; tptuqfi s ehd; gbj ; J GheJ nfhz NI d; vd; Di l a reNj fqqfi s Nfl fTk> mj wfhd j Fej tptfqqfi s ngwTk; thaggsptfpggl LssJ vd mwpeJ nfhz NI d;	<input type="text"/>
2.	ehd; , t; thapty; j d d p i rahf j hd; gqNfwfNwd; vej fhuz j j pdhNyh vej fl j j j pYk> vej r l l rpf fYk; cl gl hky; ehd; , t; thapty; , UeJ tpyfp nfhs syhk; vd; Wk; mwpeJ nfhz NI d;	<input type="text"/>
3.	, ej Ma;T rkgej khfNth> , i j r; rhheJ NkYk; Ma;T Nkwnfhs S k; NghJ k; , ej Matpy; gqF ngWk; kUj ; J th; vd; Di l a kUj ; J t mwptf fi a ghggj wF nfhs; fpNwd; ehd; Matpy; , UeJ tpyfp; nfhz l hYk; , J nghUeJ k; vd mwptfNwd;	<input type="text"/>
4.	, ej Matpd; %yk; fpi l fFk; j fti yNah> Kbi tNah gadgLj j pf; nfhs kwff khl NI d;	<input type="text"/>
5.	, ej Matpy; gqF nfhs xgGf; nfhs; fpNwd; vdfF nfhl fpggl l mwpti ufspd; gb el eJ nfhs; tJ l d; Mai t Nkwnfhs S k; kUeJ mz pfF cz i kAl d; , UgNgd; vd cWj paspf; fpNwd; vd; cl y; eyk; ghj pfpggl l hNyh> myyJ vj phghuhf toffj j j wF khwhd NehaFwp nj dgl l hNyh cl Nd , i j kUj ; J t mz papl k; nj hptpgNgd; vd cWj p mspf; fpNwd;	<input type="text"/>

gqNfwgthpd; i fnahggk/ \_\_\_\_\_, l k; \_\_\_\_\_ Nj j p \_\_\_\_\_

gqNfwgthpd; ngah; kwWk; tpyhrk;

Mathshpd; i fnahggk/ \_\_\_\_\_, l k; \_\_\_\_\_ Nj j p \_\_\_\_\_

i kak; \_\_\_\_\_

fy; tawpT , yyhj thfF (i fNui f i tj j thfS fF), J mtrpak; Nj i t

rhl rapd; i fnahggk/ \_\_\_\_\_, l k; \_\_\_\_\_ Nj j p \_\_\_\_\_

ngah; kwWk; tpyhrk; \_\_\_\_\_

## **APPENDIX - II**

### **PROFORMA FOR FINE NEEDLE ASPIRATION CYTOLOGY**

CASE NUMBER :

NAME :

AGE : SEX : Male / Female

HOSPITAL IP/OP NO :

ADDRESS OF THE PATIENT :

CONTACT PHONE NO :

CLINICAL DETAILS :

DIAGNOSIS :

INVESTIGATIONS :

TFT :

OTHERS :

PREVIOUS FNAC REPORT :

FNAC :

CYTOLOGY NO :

MACROSCOPIC APPEARANCE:

MICROSCOPY :

CELLULARITY :

CELL TYPE :

OTHER CELLS :

BACKGROUND :

DIAGNOSIS :

## APPENDIX - III

### PROFORMA FOR MASTER CHART

#### A – PATIENT PROFILE

A1	CASE NO:								
A2	IP/OP NO:								
A3	FNAC NO:								
A4	AGE	0-9	10-19	20-29	30-39	40-49	50-59	60-69	>70
		1	2	3	4	5	6	7	8
A5	GENDER	MALE				FEMALE			
		1				2			

#### B – HISTORY

##### Presenting complaints

B1	Swelling	Midline		Lateral	
	Neck	1		2	
B2	Duration of swelling	< 6months	6 – 1 yr	1 – 10 yrs	➤ 10 yrs
		1	2	3	4
B3	Rate of growth	Gradual		Sudden	
		1		2	

**Pressure effects**

B5	Dyspnoea	Present	Absent
		1	2
B6	Dysphagia	Present	Absent
		1	2
B7	Hoarseness	Present	Absent
		1	2
B8	Pain	Present	Absent
		1	2

**C. GENERAL EXAMINATION**

C1	Pulse	Bradycardia	Tachycardia	Normal
		1	2	3
C2	Skin	Dry	Moist	Normal
		1	2	3

**D . LOCAL EXAMINATION**

D1	Nodule No	Single	Multiple
		1	2
D2	Size	< 1cm	>1cm
		1	2
D3	Nature of the swelling	Nodular	Diffuse
		1	2

D4	Consistency of the swelling	Soft	Cystic	Firm	Hard
		1	2	3	4
D5	Moves with deglutition	Present		Absent	
		1		2	

### **E : FNAC FINDINGS**

E1	Nature of aspirate	Brown		Haemorrhage	
		1		2	
E2	Type of smear	Direct		Centrifuge	
		1		2	
E3	Cellularity	Sparse	Moderate		Marked
		1	2		3
E4	Background	Colloid	Haemorrhage		Inflammatory
		1	2		3
E5	Distribution of cells	Clumps	Sheets	Follicles	Papillary
		1	2	3	4
E6	Lymphocytes	Present		Absent	
		1		2	
E7	Hurthle cells	Present		Absent	
		1		2	

**F : Epithelial cell characteristics**

F1	Size			Normal		Increased
				1		2
F2	Shape	Round	Oval	Polygonal	Spindle	Plasmacytoid
		1	2	3	4	5
F3	Uniformity			Uniform		Pleomorphic
				1		2

**Cytoplasm**

F4	Amount	Abundant	Moderate	Scanty
		1	2	3
F5	Appearance	Eosinophilic	Basophilic	Vacuolated
		1	2	3

**Nucleus**

F6	Shape	Round	Oval
		1	2
F7	Ground glass	Present	Absent
F8	Hyperchromatism	Present	Absent
		1	2
F9	Nucleolus	Present	Absent



		1	2
F10	Nuclear groove	Present	Absent
		1	2
F11	Intranuclear inclusion	Present	Absent
		1	2
F12	Salt and pepper chromatin	Present	Absent
		1	2
F13	Multinucleation	Present	Absent
		1	2
F14	NC ratio	Normal	Increased
		1	2

### CONVENTIONAL CYTOLOGIC DIAGNOSIS

G1	Benign	Colloid Nodule	1
		Nodular Goitre	2
		Adenomatous goitre	3
		Hashimoto's thyroiditis	4
		Follicular Neoplasm	5
		Granulomatous thyroiditis	6
		Cystic lesion	7
		FN/ DN of nodular goitre	8

G2	Malignant	Papillary carcinoma	1
		Follicular carcinoma	2
		Medullary carcinoma	3
		Anaplastic	4
		Metastatic	5

#### **H . CYTOLOGICAL DIAGNOSIS BY BETHESDA SYSTEM**

H1	Non-diagnostic/ Unsatisfactory	Cyst fluid only	1
		Virtually acellular smear	2
		Others (Obscuring blood / drying artifact)	3
H2	Benign	Consistent with benign follicular nodule (Adenomatoid nodule , Colloid nodule)	1
		Consistent with lymphocytic (Hashimoto) Thyroiditis in proper clinical context	2
		Consistent with granulomatous (subacute thyroiditis)	3
		Other	4
H3	Atypia of undetermined significance or follicular lesion of undetermined significance		1
H4	FN/SFN		1

H5	Suspiciousfor malignancy	Suspiciuos for papillary carcinoma	1
		Suspicious for medullary carcinoma	2
		Suspicious for metastatic carcinoma	3
		Suspicious for lymphoma	4
		Other	5
H6	Malignant	Papillary thyroid carcinoma	1
		Poorly differentiated carcinoma	2
		Medullary thyroid carcinoma	3
		Undifferentiated (anaplastic) carcinoma	4
		Squamous cell carcinoma	5
		Carcinoma with mixed features	6
		Metastatic carcinoma	7
		Non – Hodgkin lymphoma	8
		Others	9

A1	A2	A3	A4	A5	B1	B2	B3	B4	B5	B6	B7	C1	C2	C3	C4	C5	D1	D2	D3	D4	D5	E1	E2	E3	E4	E5	E6	E7	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12	F13	F14	G1	G2	H1	H2	H3	H4	H5	H6
1	67746	555/13	6	2	1	1	1	2	2	2	2	3	3	1	1	1	1	2	1	3	1	1	2	2	1	1	1	2	2	1	1	1	2	1	1	2	2	2	2	2	2	2	2	2	1	1				
2	19131	558/13	5	1	2	1	1	2	2	2	2	3	3	1	1	1	3	2	2	1	1	1	1	2	1	1	1	2	2	1	1	1	2	1	1	2	2	2	2	2	2	2	2	2	1	1				
3	10480	570/13	4	2	1	3	1	2	1	2	1	3	3	1	1	1	2	1	1	1	1	1	2	1	1	1	2	1	1	2	1	1	2	1	1	2	2	2	2	2	2	2	1	1						
4	10237	571/13	6	2	1	1	2	1	2	2	2	3	3	1	1	1	1	2	1	3	1	1	2	1	1	1	2	2	1	1	1	2	1	1	2	2	2	2	2	2	2	2	1	2						
5	66487	575/13	6	2	2	2	2	2	2	2	2	3	3	1	1	1	1	2	1	3	1	1	1	2	1	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	1	1							
6	10425	582/13	4	2	2	1	1	2	1	2	2	3	3	1	1	1	3	2	2	3	1	2	1	2	2	2	2	2	2	1	2	1	1	2	2	2	2	2	2	2	2	1	2							
7	65918	587/13	3	2	2	1	2	1	2	2	2	3	3	1	1	1	1	2	2	3	1	2	1	2	1	1	2	2	2	1	2	1	1	2	2	2	2	2	2	2	2	1	2							
8	13432	612/13	3	2	2	1	2	1	2	2	2	3	3	1	1	1	1	2	1	3	1	1	1	2	1	1	1	2	2	1	1	2	2	1	1	2	2	2	2	2	2	2	1	2						
9	13477	613/13	4	2	1	3	1	2	2	2	2	3	3	1	1	1	3	2	2	3	1	1	2	1	1	2	1	1	2	2	1	1	2	2	1	2	2	2	2	2	2	2	1	2						
10	70999	619/13	7	2	2	1	2	1	2	2	2	3	3	1	1	1	1	2	1	3	1	1	2	1	3		2	2																						
11	11222	621/13	5	2	2	2	1	2	2	2	2	3	3	1	1	1	1	2	1	3	1	2	1	2	1	2	2	2																						
12	13769	627/13	2	2	2	1	2	1	2	2	2	1	1	1	1	1	3	2	2	1	1	2	1	2	3	1	1	2	2	1	1	1	2	1	1	2	2	2	2	2	2	2	1	4						
13	71606	625/13	4	2	2	1	2	2	2	2	2	3	3	1	1	1	1	2	1	3	1	2	1	2	2	2	2	2	2	1	1	2	1	1	2	2	2	2	2	2	2	2	1	2						
14	71876	625/13	8	2	2	1	1	2	2	2	2	3	3	1	1	1	1	2	1	4	1	2	1	2	5	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	1	2						
15	72122	658/13	7	1	2	2	2	1	2	2	2	3	3	1	1	1	2	1	3	1	2	1	2	2	2	2	2	2	2	1	1	2	2	1	2	2	2	2	2	2	2	2	2	1	2					
16	23310	712/13	4	2	2	2	1	2	1	2	2	3	3	3	3	2	3	2	2	1	1	2	1	2	3	3	2	2	1	1	2	2	1	2	2	2	2	2	2	2	2	2	2	1	4					
17	13573	748/13	5	2	2	1	2	2	2	2	2	3	3	1	1	1	3	2	2	3	1	1	2	2	1	1	2	2	1	1	2	2	1	1	2	2	2	2	2	2	2	2	2	1	2					
18	13609	766/13	3	2	1	2	1	2	2	2	2	3	3	1	1	1	3	2	2	3	1	1	2	1	2	2	1	2	2	1	1	2	2	1	1	2	2	2	2	2	2	2	2	1	2					
19	80580	767/13	3	2	2	1	2	1	2	2	2	3	3	1	1	1	1	2	1	3	1	2	1	2	1	1	2	2	1	1	1	2	2	1	1	2	2	2	2	2	2	2	1	2						
20	25286	803/13	5	2	1	3	1	2	1	2	2	3	3	1	1	1	2	2	1	3	1	2	1	2	3	2	2	2	2	1	1	2	2	1	1	2	2	2	2	2	2	2	2	1	2					
21	11916	804/13	6	2	1	3	1	2	1	2	2	3	3	1	1	1	2	1	1	3	1	2	1	2	2	2	2	2	2	1	2	1	2	1	1	2	2	2	2	2	2	2	2	1	3					
22	82805	812/13	3	1	2	1	2	1	2	1	2	2	3	3	1	1	1	2	2	1	3	1	2	1	2	2	2	2	2	1	1	2	2	1	1	2	2	2	2	2	2	2	2	1	3					
23	26054	834/13	5	2	2	2	1	2	1	2	2	3	3	1	1	1	1	2	1	3	1	2	1	2	2	2	2	2	2	1	1	2	2	1	1	2	2	2	2	2	2	2	2	2	1	5				
24	15104	836/13	8	2	2	1	2	1	2	1	2	3	3	1	1	1	1	1	1	3	1	2	1	2	1	3	2	4	2	2	1	1	1	1	2	2	1	2	2	2	2	2	2	2	1	3				
25	15303	840/13	4	2	2	1	2	1	2	1	2	2	3	3	1	1	1	1	2	1	3	1	2	1	2	2	2	2	2	1	1	2	2	1	1	2	2	2	2	2	2	2	2	2	1	3				
26	81656	862/13	5	1	2	2	1	2	1	2	2	3	3	1	1	1	1	3	1	2	1	2	1	2	2	2	2	2	2	1	1	2	2	1	1	2	2	2	2	2	2	2	2	1	2					
27	8919	863/13	5	2	2	1	2	1	2	2	2	3	3	1	1	1	3	2	2	3	1	2	1	2	2	2	2	2	2	1	1	2	2	1	1	2	2	2	2	2	2	2	2	2	1	2				
28	85946	864/13	5	2	1	2	1	2	2	2	2	3	3	1	1	1	1	2	1	3	2	2	1	2	2	2	2	2	2	1	1	2	2	1	1	2	2	2	2	2	2	2	2	1	2					
29	86242	865/13	7	2	2	1	2	1	2	2	2	3	3	1	1	1	1	1	1	3	1	2	1	2	2	2	2	2	2	1	1	2	2	1	1	2	2	2	2	2	2	2	2	1	1					
30	85877	867/13	5	2	1	2	1	2	1	2	2	3	3	1	1	1	1	2	1	3	1	2	1	2	1	3	2	2	2	1	1	2	2	1	1	2	2	2	2	2	2	2	2	1	1					
31	86346	868/13	4	2	2	1	2	1	2	1	2	1	1	1	1	1	3	2	2	3	1	2	1	2	1	3	3	1	2	1	1	2	2	1	1	2	2	2	2	2	2	2	2	1	4					
32	87868	890/13	2	2	2	1	2	1	2	1	2	3	3	1	1	1	1	3	2	2	3	1	2	1	3	3	1	1	2	1	1	2	2	1	2	2	2	2	2	2	2	2	2	1	6					
33	27248	896/13	2	1	2	1	2	1	2	1	2	2	3	3	1	1	1	1	2	1	2	1	2	1	2	2	2	2	1	1	2	2	1	1	2	2	2	2	2	2	2	2	2	1	3					
34	80495	901/13	4	2	2	1	2	1	2	1	2	2	3	3	1	1	1	2	1	3	1	2	1	2	2	2	2	2	1	1	2	2	1	1	2	2	2	2	2	2	2	2	1	2						
35	83527	910/13	3	2	2	1	2	1	2	2	2	3	3	1	1	1	1	2	1	1	1	2	1	2	2	1	2	2	1	1	2	2	1	1	2	2	2	2	2	2	2	2	1	2						
36	79577	911/13	4	2	2	1	2	1	2	2	2	3	3	1	1	1	1	2	2	3	1	2	1	2	2	2	2	2	1	1	2	2	1	1	2	2	2	2	2	2	2	2	1	1						
37	87460	912/13	3	2	2	1	1	2	1	2	2	3	3	1	1	1	1	2	1	2	1	2	1	2	1	2	1	2	1	1	2	1	1	2	2	2	2	2	2	2	2	2	7							
38	69290	923/13	6	2	2	3	1	2	1	2	2	1	1	3	3	1	2	3	2	2	3	1	2	1	3	3	1	1	1	1	2	1	1	2	1	1	2	2	2	2	2	2	1	4						
39	89275	924/13	5	2	2	1	2	1	2	1	2	3	3	1	1	1	2	3	1	3	1	2	1	2	2	3	1	2	2	1	1	2	2	1	1	2	2	2	2	2	2	2	1	2						
40	96724	950/13	4	2	2	1	2	1	2	1	2	1	1	3	3	2	3	2	2	3	1	2	1	2	2	3	1	1	1	2	1	1	2	1	2	2	2	2	2	2	2	2	1	4						

[illegible]

[illegible]

[illegible]





[illegible]

[illegible]